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TRANSACTIONS

OF THE

ASSOCIATION OF AMERICAN PHYSICIANS.

SEVENTH SESSION.

HELD AT WASHINGTON, D. C.,

MAY 24, 25, AND 26, 1892.

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VOLUME VII.

PHILADELPHIA:
PRINTED FOR THE ASSOCIATION.
1892.

DORNAN, PRINTER,
100 NORTH SEVENTH STREET,
PHILADELPHIA.

CONTENTS.

PAGE

List of Officers for the year 1892–93 v
List of Honorary Members vi
List of Members vii
Minutes of the Seventh Annual Meeting xi

A Bacteriological Study of Drinking-water. By VICTOR C. VAUGHAN, Ph.D., M.D., Professor of Hygiene and Director of the Hygienic Laboratory in the University of Michigan, Ann Arbor . . . 1
The Treatment of Typhoid Fever by Cold Baths. By GEORGE WILKINS, M.D., Professor of Medical Jurisprudence and Lecturer on Histology, McGill University; Physician to the Montreal General Hospital 44
A Brief Summary of the Clinical History and Treatment of Two Thousand and Twelve Cases of Alcoholism, of which Eighty-seven were Maniacal. By THOMAS S. LATIMER, M.D., of Baltimore . 62
Practical Results of Bacteriological Researches. By GEORGE M. STERNBERG, M.D., Lieutenant-Colonel and Surgeon, U. S. A. . . . 68
The Treatment of Experimental Tuberculosis by Koch's Tuberculin, Hunter's Modifications, and other Products of the Tubercle Bacillus. By E. L. TRUDEAU, M.D., of Saranac Lake, New York . 87
Mid-Systolic and Late-Systolic Mitral Murmurs. By J. P. CROZER GRIFFITH, M.D., Professor of Clinical Medicine in the Philadelphia Polyclinic; Clinical Professor of the Diseases of Children in the University of Pennsylvania 102
Dysentery. By W. T. COUNCILMAN, M.D., Shattuck Professor of Pathology in Harvard University, Boston 113
The Symptoms, Complications, and Treatment of Dysentery. By A. BRAYTON BALL, M.D., Visiting Physician to the New York Hospital and St. Luke's Hospital 141
On the Treatment of Acute Dysentery by Antiseptic Rectal and Colon Irrigation. By W. W. JOHNSTON, M.D., Professor of Theory and Practice of Medicine, Medical Department of the Columbian University; Consulting Physician to Children's, Garfield, and Emergency Hospitals, Washington, D. C. 169

PAGE

A Contribution to the Study of Hepatic Abscess. By WILLIAM C. DABNEY, M.D., Professor of Obstetrics and Practice of Medicine in the University of Virginia 181

A Case Presenting the Symptoms of Landry's Paralysis, with Recovery. By F. T. MILES, M.D., Professor of Physiology and Clinical Professor of Diseases of the Nervous System, University of Maryland 212

A Case Presenting the Symptoms of Landry's Paralysis; Recovery. By ALEXANDER MCPHEDRAN, M.D., Associate Professor of Medicine and Clinical Medicine, University of Toronto 215

Local Anæsthesia as a Guide in the Diagnosis of Lesions of the Lower Spinal Cord. By M. ALLEN STARR, M.D., Ph.D., Professor of Diseases of the Mind and Nervous System in the College of Physicians and Surgeons of New York; Consulting Neurologist to the Orthopædic, Presbyterian, and Babies' Hospitals 223

A Study of the Seasonal Relations of Chorea and Rheumatism for a Period of Fifteen Years—1876 to 1890 inclusive. By MORRIS J. LEWIS, M.D., Attending Physician to the Orthopædic Hospital and Infirmary for Nervous Diseases, the Pennsylvania, and the Children's Hospitals, Philadelphia 249

The Significance of Intermission in Functional Nervous Diseases. By W. H. THOMSON, M.D., Professor of Materia Medica, Therapeutics, and Diseases of the Nervous System in the University of the City of New York 267

Malarial Hæmaturia or Hæmoglobinuria, and the Value of Quinine in the Affection. By H. A. HARE, M.D., of Philadelphia . . 281

Misconceptions and Misnomers Revealed by Modern Gastric Research. By CHARLES G. STOCKTON, M.D., Professor of Medicine, Medical Department of the University of Buffalo 300

The Production of Tubular Breathing in Consolidation and Other Conditions of the Lungs. By CHARLES CARY, M.D., Professor of Therapeutics and Clinical Medicine in the University of Buffalo . 313

The Different Forms of Cardiac Pain. By SAMUEL C. CHEW, M.D., Professor of Principles and Practice of Medicine in the University of Maryland, Baltimore 324

Crossed Paralysis of the Thermal Sense without other Sensory Loss. By S. WEIR MITCHELL, M.D., of Philadelphia 332

Tube Casts and their Diagnostic Value. By I. N. DANFORTH, A.M., M.D., Professor of Clinical Medicine in the Chicago Medical College, and of Renal Diseases in the Woman's Medical College of Chicago 335

Report of a Case of Glanders, with Results of Bacteriological Studies. By WILLIAM PEPPER, M.D., University of Pennsylvania . . 344

ASSOCIATION OF AMERICAN PHYSICIANS

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HONORARY MEMBERS.

† Deceased.

†1890. Barker, Fordyce, M.D., New York.
1886. Billings, John S., M.D., U. S. A., Surgeon-General's Office, Washington, D.C.
†1886. Bowditch, Henry I., M.D., Boston.
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†1886. Dalton, John C., M.D., New York.
†1886. Leidy, Joseph, M.D., Philadelphia.
1886. Metcalfe, John T., M.D., 30 W. 33d St., New York.
1886. Stillé, Alfred, M.D., 3900 Spruce St., Philadelphia.

MEMBERS.

* Original members.
† Deceased members.

1892. Abbott, Alexander C., M.D., University of Pennsylvania, Laboratory of Hygiene, Philadelphia.
*1886. Adams, J. F. A., M.D., 26 Wendell Ave., Pittsfield, Mass.
*1886. Atkinson, I. E., M.D., 605 Cathedral St., Baltimore.
*1886. Ball, A. Brayton, M.D., 42 W. 36th St., New York.
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1892. Bolton, Meade, M.D., Hoagland Laboratory, Brooklyn, New York.
1890. Bond, Charles S., M.D., 112 N. 10th St., Richmond, Ind.
1888. Bridge, Norman, M.D., 217 S. Broadway, Los Angeles, Cal.
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*1886. Busey, Samuel C., M.D., 1545 I St. (N. W.), Washington, D. C.
1889. Cary, Charles, M.D., 340 Delaware Ave., Buffalo, N.Y.
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*1886. Chew, Samuel C., M.D., 215 W. Lanvale St., Baltimore.
*1886. Councilman, W. T., M.D., Johns Hopkins University, Baltimore.
1889. Dabney, William C., M.D., University of Virginia, Va.
*1886. DaCosta, J. M., M.D., 1700 Walnut St., Philadelphia.
1888. Dana, Charles L., M.D., 50 W. 46th St., New York.
*1886. Dana, Israel T., M.D., 181 State St., Portland, Me.
1888. Danforth, I. N., M.D., 294 W. Monroe St., Chicago.
*1886. Delafield, Francis, M.D., 12 W. 32d St., New York.
†1886. Donaldson, Frank, M.D., 510 Park Ave., Baltimore.
*1886. Draper, William H., M.D., 19 E. 47th St., New York.
*1886. Edes, Robert T., M.D., Adams Nervine Asylum, Jamaica Plain, Mass.

1888. Ernst, Harold C., M.D., Jamaica Plain, Mass.
1890. Fisk, Samuel A., M.D., 809 16th St., Denver, Col.
*1886. Fitz, Reginald H., M.D., 18 Arlington St., Boston.
*1886. Folsom, Charles F., M.D., 15 Marlborough St., Boston.
*1886. Forchheimer, F., M.D., 160 W. 9th St., Cincinnati.
†1886. Formad, Henry F., M.D., 3535 Locust St., Philadelphia.
*1886. Gannett, William W., M.D., 274 Marlborough St., Boston.
*1886. Garland, George M., M.D., 274 Newbury St., Boston.
1889. Geddings, W. H., M.D., Aiken, S. C.
1889. Gibbes, Heneage, M.D., 16 Forest Ave., Ann Arbor, Mich.
*1886. Graham, J. E., M.D., Gerrard St., Toronto, Canada.
1890. Griffith, J. P. Crozer, M.D., 123 S. 18th St., Philada.
*1886. Guitéras, John, M.D., 3731 Spruce St., Philadelphia.
1890. Hare, Hobart A., M.D., 222 S. 15th St., Philadelphia.
*1886. Hays, I. Minis, M.D., 266 S. 21st St., Philadelphia.
*1886. Henry, Frederick P., M.D., 1635 Locust St., Philada.
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†1886. Hutchinson, James H., M.D., Philadelphia.
*1886. Jacobi, A., M.D., 110 W. 34th St., New York.
*1886. Janeway, E. G., M.D., 36 W. 40th St., New York.
†1886. Johnson, Hosmer A., M.D., Chicago.
*1886. Johnston, W. W., M.D., 1603 K St. (N. W.), Washington, D. C.
*1886. Kinnicutt, Francis P., M.D., 42 W. 37th St., New York.
1890. Latimer, Thomas S., M.D., 103 W. Monument St., Baltimore.
1888. Lewis, Morris J., M.D., 1316 Locust St., Philadelphia.
*1886. Loomis, Alfred L., M.D., 19 W. 34th St., New York.
1889. Loving, Starling, M.D., 229 E. State St., Columbus, Ohio.
*1886. Lusk, William T., M.D., 47 E. 34th St., New York.
*1886. Lyman, Henry M., M.D., 65 Randolph St., Chicago.

†1886. McBride, Thomas A., M.D., New York.
†1890. MacDonnell, R. L., M.D., Montreal, Canada.
1891. McPhedran, A., M.D., 84 College St., Toronto, Canada.
1891. Mason, A. Lawrence, M.D., 265 Clarendon St., Boston.
1887. Meigs, Arthur V., M.D., 1322 Walnut St., Philadelphia.
1892. Meltzer, S. J., M.D., 66 East 124th St., New York.
*1886. Miles, F. T., M.D., 514 Cathedral St., Baltimore.
*1886. Minot, Francis, M.D., 65 Marlborough St., Boston.
*1886. Mitchell, S. Weir, M.D., 1524 Walnut St., Philada.
1887. Musser, John H., M.D., 40th and Locust Sts., Philada.
1891. Northrup, W. P., M.D., 57 E. 79th St., New York.
1892. Nuttall, George H. F., M.D., Johns Hopkins University, Baltimore.
*1886. Osler, William, M.D., Johns Hopkins Hospital, Baltimore.
*1886. Peabody, George L., M.D., 57 W. 38th St., New York.
*1886. Pepper, William, M.D., 1811 Spruce St., Philadelphia.
*1886. Polk, William M., M.D., 7 E. 36th St., New York.
1888. Prentiss, D. W., M.D., 1101 14th St. (N. W.), Washington, D. C.
*1886. Prudden, T. Mitchell, M.D., 23 W. 33d St., New York.
1889. Purdy, Charles W., M.D., 163 State St., Chicago.
*1886. Putnam, James J., M.D., 106 Marlborough St., Boston.
1887. Reeves, James E., M.D., 201 McCallie Ave., Chattanooga, Tenn.
*1886. Robinson, Beverley, M.D., 37 W. 35th St., New York.
*1886. Robinson, P. G., M.D., 3411 Washington Ave., St. Louis.
†1886. Rochester, Thomas F., M.D., Buffalo, New York.
1889. Roosevelt, J. West, M.D., 32 E. 31st St., New York.
*1886. Ross, George, M.D., 49 Union Ave., Montreal, Canada.
†1886. Schmidt, H. D., M.D., New Orleans, La.
*1886. Seguin, E. C., M.D., 419 Madison Ave., New York.
*1886. Shakespeare, Edward O., M.D., 1336 Spruce St., Phila.
*1886. Shattuck, Frederick C., M.D., 125 Marlborough St., Boston.
*1886. Shattuck, George B., M.D., 24 Marlborough St., Boston.
*1886. Sinkler, Wharton, M.D., 1606 Walnut St., Philada.
*1886. Smith, A. A., M.D., 40 W. 47th St., New York.

1891. Smith, Andrew H., M.D., 22 E. 42d St., New York.
1892. Smith, Theobald, M.D., Washington, D. C.
*1886. Solly, Edwin S., 2 N. Cascade Ave., Colorado Springs, Col.
1887. Starr, Louis, M.D., 1818 S. Rittenhouse Square, Philada.
1887. Starr, M. Allen, M.D., 22 W. 48th St., New York.
*1886. Sternberg, George M., M.D., U. S. A., Johns Hopkins University, Baltimore.
*1886. Stewart, James, M.D., 939 Dorchester St., Montreal, Canada.
1889. Stockton, Charles G., M.D., 436 Franklin St., Buffalo, N. Y.
†1886. Thacher, James K., M.D., New Haven, Conn.
1889. Thompson, W. Gilman, M.D., 49 E. 30th St., New York.
1889. Thomson, William H., M.D., 7 W. 56th St., New York.
*1886. Trudeau, Edward L., M.D., Saranac Lake, Franklin Co., N. Y.
*1886. Tyson, James, M.D., 1506 Spruce St., Philadelphia.
1889. Vaughan, Victor C., M.D., University of Michigan, Ann Arbor, Mich.
1889. Walcott, Henry P., M.D., 11 Waterhouse St., Cambridge, Mass.
*1886. Ward, Samuel B., M.D., 135 N. Pearl St., Albany, N. Y.
*1886. Welch, William H., M.D., 506 Cathedral St., Baltimore.
1889. Westbrook, B. F., M.D., 174 Clinton St., Brooklyn, N.Y.
*1886. Whittaker, James T., M.D., 100 Garfield Place, Cincinnati.
*1886. Wilkins, George, M.D., 898 Dorchester St., Montreal, Canada.
*1886. Wilson, James C., M.D., 1437 Walnut St., Philadelphia.
*1886. Wood, Horatio C., M.D., 1925 Chestnut St., Philadelphia.

MINUTES

OF THE

SEVENTH ANNUAL MEETING,

Held at Washington, D. C., May 24, 25, and 26, 1892.

Tuesday, May 24th.

Morning Session.

The Association met in the Army Medical Museum and Library Building, and was called to order at 10.30 o'clock by the President, Dr. Henry M. Lyman.

In the absence of the Secretary, Dr. I. Minis Hays was appointed Secretary *pro tem.*

The following members were present:

J. F. A. Adams.
I. E. Atkinson.
A. Brayton Ball.
John S. Billings.
Samuel C. Busey.
Charles Cary.
Samuel C. Chew.
W. T. Councilman.
William C. Dabney.
Israel T. Dana.
George M. Garland.
J. P. Crozer Griffith.
Hobart A. Hare.
I. Minis Hays.
Frederick P. Henry.
Henry Mills Hurd.
Abraham Jacobi.
W. W. Johnston.
Francis P. Kinnicutt.
Thomas S. Latimer
Morris J. Lewis.
Starling Loving.
Henry M. Lyman.
A. McPhedran.
A. Lawrence Mason.
Arthur V. Meigs.
F. T. Miles.
S. Weir Mitchell.
John H. Musser.
William Osler.
William Pepper.
D. Webster Prentiss.
Louis Starr.
M. Allen Starr.

George M. Sternberg.	James Tyson.
Charles G. Stockton.	Victor C. Vaughan.
W. Gilman Thompson.	William H. Welch.
William H. Thomson.	George Wilkins.

The minutes of the sixth annual meeting, on motion, were accepted as printed, and their reading omitted.

The Secretary presented a letter from Dr. J. S. Billings, stating that he had been authorized by the Surgeon-General of the Army to extend the hospitality of a room at the Army Medical Museum for the Seventh Annual Meeting of the Association, which he did with great pleasure. On motion of Dr. Pepper, it was moved that the Secretary transmit to the Surgeon-General the best thanks of the Association for the courtesy wihch he had extended to it.

The President, Dr. Lyman, then delivered the following

Annual Address.

It is with great pleasure that I find myself once more at a meeting of the Association of American Physicians, and the recollection of my absence from the last meeting enables me to realize more clearly than ever the loss that is experienced through such a failure of attendance. To an isolated student these annual meetings afford intellectual refreshment and instruction which can be fully appreciated only when deprived of their sustaining power.

You have already, no doubt, remarked the absence of our efficient Secretary, Dr. Hun; obedient to the higher impulses of his being, he has taken unto himself a wife, and departed to the happy hunting-grounds of European seclusion. This incident might have been attended with deplorable consequences to the Association had not our friend Dr. Hays so kindly consented to fulfil the many exacting duties which fall to the lot of the Secretary. Aided by his presence and counsels, I feel confident that no duty pertaining to this meeting will be neglected.

Since the date of our last reunion death has removed two of the members of this Association: Dr. Francis Donaldson died in Baltimore, Maryland, after a period of declining health which was suddenly terminated by heart-failure on the morning of December 9, 1891. He had reached the age of sixty-eight years, having been born in Baltimore, July 23, 1823. The story of his life covers everything of interest pertaining to medicine in his native city during the past half-century. He was a graduate of the University of Maryland, and a pupil of the

physicians who were most eminent during his early life. After a period of practical experience as resident student in the hospitals of Baltimore, he enjoyed the advantages of clinical instruction in Paris during the year 1851. From that date he was actively employed as attending physician to the Baltimore Almshouse Hospital, to the General Dispensary of the city, and for a part of the time as resident physician at the Maryland Hospital. From 1863 to 1866 he was the Professor of Materia Medica in the Maryland College of Pharmacy, a position from which he was advanced to be Professor of Physiology and Hygiene and Clinical Professor of Diseases of the Throat and Chest in the University of Maryland. In 1880 the state of his health rendered it necessary for him to resign his active duties, and he was made emeritus professor of the branches in which he had given instruction with such brilliant success. A frequent contributor to medical periodicals, and an accomplished teacher, he was an honored member of the consulting staff of the Johns Hopkins Hospital, and at the time of his death he was connected with the American Climatological Association, the American Laryngological Association, and the Association of American Physicians. He was one of the finest types of the energetic, accomplished, and thoughtful men who adorned the last generation of American physicians.

On January 14, 1892, in the eighty-fourth year of his age, Dr. Henry Ingersoll Bowditch died in the city of Boston. Son of the celebrated mathematician, Nathaniel Bowditch, he was born in Salem, Mass., August 9, 1808. In early boyhood he removed with his father's family to Boston, and in that city of his adoption he resided until the day of his death. As a school-boy and a student at Harvard College, where he graduated in 1828, he was remarkable for all the best characteristics, physical, mental, and moral, of the New England youth of that period. Immediately after his graduation at Harvard he entered the medical school in Boston, and received the degree of M.D. in 1832, after a term of residence as house physician in the Massachusetts General Hospital. He then proceeded to Paris, and spent the greater part of two years under the instruction of the famous French teachers, Andral, Chomel, and Louis. From these eminent pioneers of modern medical science he acquired the rudiments of that power of acute observation and accurate inference that was so conspicuous a feature of his after-life. From the year 1838 until the close of his active career he was intimately connected with the Massachusetts General Hospital, the Boston City Hospital, the Carney and the New England Hospitals, in the city of his residence. When, as a medical student, in the years 1858 and

1859, I walked the wards of the Massachusetts General Hospital, Dr. Bowditch was the attending physician on duty in the hospital; I well remember the lithe and wiry form, the prematurely gray hair, and the piercing eager glance of the energetic teacher, who, after leading us from bed to bed, was in the habit of marshalling the class in the didactic room of the hospital for the purpose of reviewing the cases that he had just exhibited. The thoughtful and luminous manner with which he commented upon each morning's work was indeed an admirable model for the young students under his care. His style was plain, straightforward, and characterized by qualities that implied the possession of an unlimited fund of good sense on the part of its author.

Not only as a physician, but as a man of general information and broad sympathies, did Dr. Bowditch live among his fellow-citizens; he used to urge upon his students the importance of carrying on, in connection with their medical studies, some other branch of intellectual research in order to prevent the inevitable narrowing of the mental horizon that must follow exclusive application to a single branch of scientific investigation. Although a member of all the leading medical societies in Boston, and of the Societies of Obstetrics and of Public Hygiene, in Paris, and an honorary member of the principal medical societies in New York, Philadelphia, Rhode Island, and Connecticut, including also the American Medical Association, he found time for intellectual profit in membership of the American Academy of Arts and Sciences, and other literary and philanthropic associations in Boston. He was one of the earliest and most prominent advocates of sanitary science and public sanitation; and, after the creation in Massachusetts of the first State Board of Health ever known in this country, he devoted ten of the best years of his life to the arduous labors of its presidency. Time will not permit the enumeration of the numerous essays and pamphlets that fell from his pen; more than ninety thousand manuscript pages of records, derived from observation of cases in his private practice, were accumulated during his industrious life. As a man, as a citizen, as a physician, no purer, brighter, nobler spirit has ever adorned the medical profession.

The past year has not been particularly fruitful in brilliant discoveries within the field of medicine. Medical progress can advance only as the allied sciences pave the way by discoveries that can be utilized for the explanation of physiological and pathological phenomena, thus rendering possible new investigations in therapeutics. For these reasons it is highly important that we should carefully follow the course of research in all departments of scientific investigation. It is, there-

fore, with great satisfaction that I have remarked the activity that has characterized our fellow-laborers in these departments. During the past year a number of beliefs that were previously held upon hypothetical grounds have been subjected to the final test of experimental evidence, thus enlarging the field in which the uniform operation of the laws of physics and chemistry has been demonstrated. I will not delay the Association by anything more than a reference to the fascinating researches in the realm of astronomy which have been so recently accomplished by the aid of photography and the spectroscope. To us the principal interest lies in the demonstration thus afforded of the unity of type and method in all the cosmic movements of matter, enabling us to read in the language of the stars the past history and the future course not only of our own solar system, but of the planet upon which we dwell.

The experiments in electricity that were announced three years ago by Professor Hertz, of Carlsruhe, have continued to bear fruit during the past year. It may be now assumed as experimentally demonstrated that electricity, as well as light and heat, are what they have been long supposed to be, modes of motion in an all-pervasive ether. By this demonstration we are brought one step nearer towards the complete definition of the antithesis between mind and matter.

Among the biologists, during the past year, research has been particularly occupied with the investigation of the elementary composition and attributes of protoplasm. In connection with the questions that bear upon the subject of heredity many interesting observations have been published; the investigations of Strasburger, Flemming, Guignard, and Fol have thrown new light upon the phenomena of fecundation and reproduction, giving reason to hope that in no very distant future the problems of heredity may receive a satisfactory solution. Another important question regarding the ultimate organization of protoplasm itself is gradually approaching its solution: two rival hypotheses at present occupy the field—Altman (*Die Elementar-Organismen und ihre Beziehungen zu den Zellen*, Leipzig, 1890), Straus (*Sur la morphologie de la cellule bacterienne*, *Journal de Micrographie*, t. 15, October 25, 1891), and Vogt (*Das Empfindungsprinzip und das Protoplasma, auf Grund eines einheitlichen Substanzbegriffes*, Leipzig, 1891; Journal of the Microscopical Society, February, 1892), are of the opinion that cell-protoplasm is to be considered as an aggregation of coördinated elementary organisms that bear to the animal or vegetable cell a relation not unlike that of independent microbes. The constituent cells of the tissues, according to this hypothesis, are sup-

posed to be made up of aggregations of a micro-zoic or micro-phytic nature, which differ from ordinary bacteria and protozoa only by their smaller dimensions and their capacity for coördinate activity. The bearing of such speculations upon the facts of infection and of fecundation is quite obvious. On the other hand, Bütschli maintains that it is entirely unnecessary to assume the existence of any special co-ordinating force, and is of the opinion that all the phenomena which are exhibited by protoplasm may be produced by the operation of ordinary chemical and physical forces.

The past year has been distinguished by the completion of the new edition of Eichhorst's great work on *Internal Medicine*, and by the appearance of the first two volumes of the French *Traité de Médecine*. In our own country, our associate, Osler, has laid upon us all a debt of gratitude for his admirable volume on the *Practice of Medicine*. I trust that I may be permitted to congratulate our fraternity upon these epoch-making achievements, especially since they indicate the complete recuperation of the French school of medicine from the stunning shock of the Franco-Prussian war. The consecutive volumes of Eichhorst remind one of the invincible German infantry, ponderous, thoroughly trained, and invincible, but war-worn and weather-stained to the last degree. Turning from these serried ranks to the French side of the line, we find all the pomp and circumstance of war, all the glitter of gold, the splendor of apparel, the *élan* and *esprit* that have always characterized the French nation. Judging from the already published volumes, the new *Traité de Médecine* will be, when completed, the most valuable contribution to the literature of internal medicine that has been yet produced. The world certainly cannot yet dispense with the services of the French any more than it can do without the Germans.

Dr. Victor C. Vaughan read a paper on "The Bacteriological Study of Drinking-Water," which was discussed by Drs. Sternberg, Welch, Pepper, and Vaughan.

Dr. G. Wilkins read a paper on "The Cold-Water Treatment of Typhoid Fever," which was discussed by Drs. Osler, Kinnicutt, Pepper, Atkinson, W. G. Thompson, Tyson, Stockton, and Wilkins.

Dr. William Pepper read by title a paper entitled a "Report of a Case of Glanders, with Results of Bacteriological Study."

Afternoon Session.

Dr. George M. Garland read by title a paper on "The Treatment of Follicular Tonsillitis."

Dr. T. S. Latimer read a paper on "Alcoholism," which was discussed by Drs. Osler and Garland.

Dr. George M. Sternberg read a paper entitled "Practical Results of Bacteriological Researches," which was discussed by Drs. Welch, Kinnicutt, Vaughan, Lyman, and Sternberg.

Dr. E. L. Trudeau presented a paper on "The Treatment of Experimental Tuberculosis by Koch's Tuberculin, Hunter's Modifications, and other products of the Tubercle Bacillus," which was read by Dr. Welch and discussed by Drs. Kinnicutt and Welch.

Dr. Pepper moved that the rules be suspended so that the hour of 12, on May 25th, be assigned as the time when the executive business of this meeting be transacted. Adopted.

Dr. W. W. Johnston presented the Treasurer's annual report, which was referred to an Auditing Committee, consisting of Drs. Israel T. Dana and Louis Starr.

Dr. J. P. Crozer Griffith read a paper on "The Mid-Systolic and Late-Systolic Mitral Murmurs," which was discussed by Dr. Garland.

Wednesday, May 25th.

Morning Session.

The session was called to order at 10 A. M. by the President. A discussion on "Dysentery" was opened by Dr. W. T. Councilman as referee, who read a paper on the "Etiology and Pathology," and Dr. A. Brayton Ball, as co-referee, read a paper on the "Symptomatology," Complications, and Treatment."

Dr. W. W. Johnston read a paper on the "Treatment of Acute Dysentery by Antiseptic Colon and Rectal Irrigation."

Dr. W. C. Dabney presented "A Contribution to the Study of Hepatic Abscess."

The Association then went into

Executive Session

for the transaction of private business.

The Auditors reported that they had examined the Treasurer's report, compared the same with the vouchers, and had found it correct, showing a balance in hand of $1431.03.

Drs. M. Allen Starr and J. P. Crozer Griffith were appointed tellers

to conduct the election, and they reported that the following had been unanimously elected as *Officers for the ensuing year:*

President.—Alfred L. Loomis.

Vice-President.—Reginald H. Fitz.

Recorder.—I. Minis Hays.

Secretary.—Henry Hun.

Treasurer.—William W. Johnston.

Member of Council.—A. Brayton Ball.

Representative on Executive Committee of the Congress of American Physicians and Surgeons.—William Pepper.

And that the following were elected to *membership:*

S. J. Meltzer, of New York.

G. H. F. Nuttall, of Baltimore.

Alexander C. Abbott, of Philadelphia.

Meade Bolton, of Brooklyn.

Theobald Smith, of Washington.

The following amendments to the Constitution were presented.

In Article VIII. insert in the sixth line after the word "publications:" "The Council shall report the name of each nominee to the members of the Association by letter prior to acting upon the same." Signed by H. A. Hare, Arthur V. Meigs, A. Jacobi, Weir Mitchell, J. H. Musser.

In Article IX. strike out "fifteen dollars," and insert "such sum as the Council from time to time may fix." Signed by W. W. Johnston, I. Minis Hays, William Pepper, W. H. Welch, S. C. Busey.

Afternoon Session.

Dr. F. T. Miles reported "A Case Presenting the Symptoms of Landry's Paralysis, with Recovery."

Dr. A. McPhedran reported "A Case Showing Symptoms of Landry's Paralysis—Recovery." These papers were discussed by Drs. Cary and W. H. Thomson.

Dr. M. Allen Starr read a paper on "The Areas of Anæsthesia in Spinal Cord Lesions as a Guide to Localization," which was discussed by Drs. Mitchell, Miles, and Starr.

Dr. Morris J. Lewis presented "A Study of the Seasonal Relations of Chorea and Rheumatism for a Period of Fifteen Years," which was discussed by Drs. Starr, Mitchell, Henry, Jacobi, Lyman, Lewis, W. H. Thomson, and Musser.

Dr. W. H. Thomson read a paper on "The Significance of Intermission in Functional Nervous Diseases."

Dr. S. Weir Mitchell read by title a paper "On Crossed Paralysis of the Thermal Sense Without Other Sensory Loss."

Dr. H. A. Hare presented "A Collective Investigation in regard to the Value of Quinine in Malarial Hæmaturia or Malarial Hæmoglobinuria," which was discussed by Drs. Atkinson, Tyson, Stockton, Henry, Vaughan, Loving, and Hare.

Thursday, May 26th.

Morning Session.

The session was called to order at 10 A. M. by the President.

The following papers were read by title:

"On Pulsating Pleural Effusions," by James C. Wilson, M.D.

"On Tube-Casts and Their Diagnostic Value," by I. N. Danforth, M.D.

Dr. Charles G. Stockton read a paper on the "Misconceptions and Misnomers Revealed by Modern Gastric Research," which was discussed by Drs. Musser and Lyman.

Dr. Charles Cary read a paper on "The Production of Tubular Breathing in Consolidation and Other Conditions of the Lungs," which was discussed by Drs. Tyson, Mason, Hare, Griffith, Lyman, Hurd, and Cary.

Dr. Samuel C. Chew read a paper on "The Different Forms of Cardiac Pain," which was discussed by Drs. M. Allen Starr, Musser, McPhedran, Stockton, and Chew.

Adjourned at 12.10 P. M.

I. Minis Hays, *Secretary pro tem.*

NOTICE.

The Association assumes no responsibility for the statements and opinions expressed in the papers read at its meetings.

A BACTERIOLOGICAL STUDY OF DRINKING-WATER.

By VICTOR C. VAUGHAN, Ph.D., M.D.,

PROFESSOR OF HYGIENE AND DIRECTOR OF THE HYGIENIC LABORATORY IN THE UNIVERSITY OF MICHIGAN, ANN ARBOR.

Since the opening of the Hygienic Laboratory of Michigan University, October 1, 1888, a large portion of my time, devoted to laboratory work, has been given to the bacteriological study of drinking-water. While I have no great discovery to announce to you, I have thought that a brief record of the results obtained after three and one-half years of work might not be wholly devoid of interest.

Health officers are given the privilege of sending samples of food and drink to the laboratory for examination, where the work is done for a small fee, which is supposed to cover the cost of material. I have been anxious from the first that this work should be of practical benefit to the people for whom it has been done, and that it should also constitute a contribution to science. Having had, before beginning this work, some years of experience in the chemical analysis of drinking-water, and having been convinced of the inadequacy of the evidence furnished by the same, I have intrusted that part of the work, in most instances, to trained assistants, and I am sure that whatever its value may be, the work has been well done. Dr. F. W. Brewer and A. Ives have made most of the chemical analyses, which will be reported in part later in this paper. A small number of the chemical examinations, and all of the bacteriological work has been done by myself, and I alone am responsible for any errors which may be detected in the same.

We keep at the laboratory a number of sterilized bottles with glass stoppers, and of two and one-half litres capacity. These bottles are sterilized by steam, then set in wooden crates so arranged that the handle of the crate holds the stopper in place, and makes it impos-

sible to open the bottle without removing the handle, which is fastened by means of screws. The use of sealing wax is forbidden, and in cases where the overzealous collector has resorted to this method "to make things more secure," the samples have been discarded and fresh bottles have been sent, with the request that the sealing be omitted. In some instances a piece of sublimate gauze has been placed over the stopper and fastened about the neck of the bottle. This admits of the collector placing his seal upon the outside of the gauze. A health officer writes or telegraphs that he wishes one or more samples examined, and the desired number of bottles is sent. He is instructed to fill them and to return them immediately. In the great majority of cases the bacteriological examination has been begun at the laboratory within thirty-six hours after the samples have been collected. In some instances I have instructed the collector to obtain new bottles and to sterilize them, but as a rule this is not satisfactory, and many samples have been discarded on learning the method of sterilization employed; the above-described method is now exclusively used.

Immediately on receipt of the water at the laboratory, gelatin plates are made, and at the same time from two to six beef-tea tubes are inoculated with the water, and placed in an incubator at 38° C. The temperature at which these beef-tea tubes are kept is, as we shall see, a matter of importance. The amount of water added to the gelatin and beef-tea tubes has varied from one drop to one cubic centimetre. My experience has led me to prefer from three to six gelatin plates, each made with one drop of water, to one plate made with one cubic centimetre, provided that in the making of each plate a drop of water is taken up in a fresh pipette after shaking the water in the bottle. I am convinced that in this manner one is less likely to fail to get on the plates all the germs in the sample of water.

After the beef-tea tubes have stood in the incubator at 38° for twenty-four hours, it is observed whether or not any germs have developed, and a record is made of this observation. As we shall see further on, the greater number of germs found in drinking-water do not multiply at all, or do so very feebly, at 38° C. Whether the germs have developed or not, animals are inoculated with the beef-tea cultures. If certain germs be present, some of the animals thus inoculated will die within a period of time which varies with

the animal employed and the method of inoculation. Practically I have used in my routine work, in the majority of instances, white rats. The reasons for selecting this animal are the following: 1. The rat is easily kept and multiplies rapidly, and where one uses from three to four hundred animals in a year, this becomes a matter of some importance. If the animal does not die, it is not used in testing other samples of water, because of the fear that a tolerance for certain water germs may have been established. Some special experiments, however, recently made to test this point, seem to show that I have overestimated this danger. 2. As compared with mice, and even with guinea-pigs and rabbits, the operation of inoculation *per se* has less effect upon the rat.

In the routine work, I have usually inoculated the rat by the injection of from one to two cubic centimetres of the beef-tea culture into the abdominal cavity. The reasons for selecting this method of inoculation are: 1. The greater certainty of killing, providing a toxicogenic germ is present, and, 2, the shortening of the length of time between the inoculation and death. These very reasons, however, which have led me to select this animal and the mode of inoculation in making the first rough test of the water, have also induced me to repeat the inoculations, using other animals and other methods of inoculation, in all cases where the results obtained by the routine tests were positive. I will give later on in detail the results of some of these inoculations.

If the animals die, plates are made from the spleen, liver, and kidneys, in *all* instances, and from the blood in some. The germs which develop on the plates made from these organs are compared with those on the plates made directly from the water, and tube cultures are made of all germs. In the majority of examinations, each germ has been studied sufficiently to enable me to identify it. The number of germs on the plates made directly from the water are counted after twenty-four, forty-eight, and seventy-two hours, and as some plates have always been made with one drop of the water, the number on these plates is given in the table.

I have used the word "toxicogenic" in referring to those germs found in drinking-water which prove fatal to inoculated animals. I have, also, elsewhere employed the same term in referring to certain other germs. The word toxicogenic (poison-producing) explains

itself, but it may be asked why I have taken the liberty of coining such a word, and exactly what meaning do I attach to it? How does it differ in meaning from pathogenic? I suppose that all now believe that germs which are harmful when introduced into the bodies of men and the lower animals owe their deleterious effects to certain chemical products which they elaborate. Therefore, all pathogenic germs are toxicogenic, but are all toxicogenic germs pathogenic? The answer to this question depends upon the meaning which one attaches to the word pathogenic. I prefer to use this word in the sense indicated by its derivation—*i. e.*, as disease-producing. Now, there are poison-producing germs which are fatal to man and some of the lower animals which are not known to induce any characteristic symptoms or any specific lesions. They grow and multiply in the body, sometimes with fearful rapidity, and prove speedily fatal.

Such are the germs which induce the great variety of symptoms which we designate as the summer diarrhœas of infancy, and which would more properly be called milk poisoning. In the same class are those germs which cause serious results to follow the eating of sausage, cheese, canned salmon, lobster, etc. These germs, it seems to me, should not be said to be pathogenic, but they certainly are toxicogenic. Now, I find in drinking-water a number of germs differing from one another morphologically and in their growth on various nutritive media, which do not, in the animals upon which I have experimented, induce any specific disease which can be recognised either by symptoms during life or by lesions after death. These germs I call toxicogenic. A germ, in order to be toxicogenic to a given animal, must multiply in the body of the animal and there elaborate its poison. In this way a germ may be toxicogenic to one animal and not to another.

We must distinguish between the germs which kill by virtue of the chemical poisons which they produce outside the body and those which produce chemical poisons within the body. This difference may be well illustrated by some of the water germs. If we allow the white liquefying bacillus of water to grow in beef-tea for some days at the ordinary temperature of a room, and then inject three or four cubic centimetres of the culture into the abdominal cavity of a white rat, the animal will succumb within a few hours. But this bacillus will not multiply at the temperature of the rat's body, and

the fatal effects are due solely to the chemical poisons which the germ produced in the beef-tea before the inoculation. The truth of this may be demonstrated by filtering the culture through a Chamberland filter, and it will be found that the same amount of the germ-free filtrate will kill. I would not say that this germ is toxicogenic to the rat, and I have been careful in all of my experiments to avoid mistaking such a germ for those which I, in this paper, designate as toxicogenic germs. In the routine work this danger is avoided by keeping my beef-tea culture in an incubator, the temperature of which will not fall below 38° C. Moreover, in order to satisfy myself that even when the germ is grown at this temperature, the fatal effects are not due to poisons generated in the tube, I have injected cultures which have been freed from germs by filtration through porcelain, and have found that six times the fatal quantity of the germ-containing cultures may be injected without fatal effect. Thus, one cubic centimetre of a beef-tea culture of bacillus venenosus twenty-four hours old invariably kills white rats, while six cubic centimetres of the same culture after filtration fails to cause death. It is true that a small amount of poison is produced in the tube, and this probably has some influence in slightly lowering the vitality of the animal, while the germ rapidly multiplies and produces a sufficient quantity of poison to cause death.

With the method of work now understood, I will give the conclusions which I have reached concerning the value of a bacteriological examination of water, and then will close with tabular statements of the investigations upon which these conclusions are based.

Some of the conclusions which have been reached in this study are as follows:

1. Many of the germs found in the drinking-water will not grow at the temperature of the human body. These germs, therefore, are not capable of inducing disease. It matters not how rich a given sample of water may be in these germs, if it contain no others it cannot be said that the water is a source of typhoid fever. The freedom from typhoid fever of communities using such waters seems to justify this conclusion. Such a water may not be, and certainly often is not, a desirable drinking-water. It may be turbid with suspended matter, unpleasant to the taste, and give off a disgusting odor, but there is no evidence that it can cause disease.

Several interesting examples of this kind have come under observation. One of these may be mentioned. A certain city of about ten thousand inhabitants took for a while its public water supply from a shallow lake, the bottom of which was covered with decomposing organic matter of vegetable origin. This water was turbid, unpleasant to the taste, and gave off unpleasant odors, but none of the bacteria in it grew at 38° C. On the other hand, many of the inhabitants of the city took their drinking-water from shallow wells, the water of which was clear, sparkling, and palatable. The well water, however, contained germs which grew abundantly at 38° C., and which were toxicogenic to animals. The use of the lake water in preference to that supplied by the wells was recommended early in the spring of 1891. Some followed the advice, others did not. During the summer and early fall of 1891 there were more than two hundred cases of typhoid fever in the city, and at a public meeting held by the State Board of Health in this place, about the last of October, every physician in the city agreed to the statement that there had not been a case of typhoid fever among those who had used the lake water exclusively. This positive testimony of the physicians was also confirmed by other citizens.

2. Of the germs which grow at 38° C. or at higher temperatures, some are fatal to animals when injected subcutaneously, while others are not. This renders a division of them into toxicogenic and non-toxicogenic germs possible.

3. There is no proof that these non-toxicogenic germs can multiply in the animal body. Indeed, all the evidence which has been gathered so far goes to show that they not only fail to multiply in the bodies of the rat, mouse, guinea-pig, and rabbit, but that they soon die when injected under the skin or into the abdomen. However, this does not furnish positive evidence that they would not multiply in the body of man. For these reasons waters containing these germs have not been positively condemned, though it has been advised in some cases that their use should be discontinued.

4. Some of the toxicogenic germs found in drinking-water produce the same symptoms and the same post-mortem appearances in the above-mentioned animals as are observed after the similar employment of Eberth's germs. Moreover, their toxicogenic properties, as tested upon these animals, are fully equal to those of Eberth's germ.

They will not only live, but will multiply in the animal body. Waters containing these germs have in all cases been condemned.

5. More than one germ obtained from drinking-water grows, with an invisible growth, on potato.

6. Several germs found in drinking-water will grow on the media proposed by Parietti, Uffelmann, and others, as means of recognition of the Eberth germ.

The results of the examination of one hundred and forty-eight waters are given in the table. The waters are divided into three classes. The *first* contains those which are supposed to be causing typhoid fever at the time the water is sent, or to have caused the disease prevailing at the time. In other words, the water has been sent on account of the present existence of typhoid fever among those using it. In the *second* class are those waters which are not supposed to be causing typhoid fever at the time, but which are suspicious on account of unsanitary surroundings, or on account of previous sickness among those drinking it. In the *third* class are given those waters which have not been suspected of causing sickness, and the sanitary surroundings of which are not said to be especially bad. Several of the third class have been sent for analysis in view of their possible selection for the water supply of cities and villages.

The figures given in the chemical part of the table represent parts per million, the chlorine being calculated as sodium chloride. The chemical analyses are much more extensive than shown in the table. I have given the results of the estimation of free and albuminoid ammonia and chlorine, because much importance has generally been attached to these by chemists. In addition to the figures given in the table a record is made of the physical properties, hardness, amount of residue organic or inorganic, sulphates, earthy bases, nitrates, nitrites, and amount of oxygen consumed in the permanganate process.

The number of germs in one drop of the water is given. In the column "kind of germ," the figures refer to the corresponding ones given in the descriptive tables of the individual germs, found later on. The germs which are indicated by the letters C, D, and E, are not given in the descriptive tables, because the cultures have been lost through negligence in not transplanting as often as should have been

done. I have elsewhere[1] described these germs, and the following is a brief description of them:

Bacillus C rapidly liquefies gelatin, the liquefaction beginning at the surface. It forms gas, is stained by the ordinary agents and by Gram's method. It resembles Eberth's germ in the formation of an invisible growth on potato, but in no other respect. Some twenty rats were killed with this germ. The minimum fatal amount of the twenty-four hours' culture for white rats seemed to be between ten and fifteen drops. One strange observation was made. Cultures nine or ten days old are apparently less virulent than those only twenty-four hours old. Moreover, the germ decreases in virulence as it is grown in the artificial media, until in about the sixth generation it may be employed in four times the quantity first used without any effect. The post-mortem appearances are quite different from those observed with Nos. 29 and 31, as given in the descriptive tables in this paper. The intestines are reddened, but the liver and spleen are tarry black. Cultures from these organs show numerous liquefying colonies.

Bacillus D is probably not pathogenic, but kills on account of the chemical poisons rapidly developed. Further study of this germ is needed before extended statements can be made concerning it. I can only say that it does not correspond with any germ given in the tables of Eisenberg.

Bacillus E is non-liquefying. It grows slowly in stick cultures, and forms a scarcely visible growth on potato. It decreases in virulence with artificial cultivation, and while none of the other germs in these waters showed any pathogenic properties in pure cultures, beef-tea inoculated with a drop of the water never failed to kill rabbits and rats, while bacillus E in pure cultures frequently failed to produce death. Moreover, after the death of these animals inoculated with the mixed culture, bacillus E was the only germ found living in the organs. The following quotation from my notes will illustrate this: October 28, 1889, a large rabbit was inoculated with sixty drops of beef-tea, to which one drop of the Negaunee public water had been added. October 31, animal found dead at 9 A.M. Post-mortem showed small intestines and mesentery highly inflamed; no other changes observable. Plates made from spleen, liver, and

[1] The Medical News, June 14, 1890.

kidney showed pure culture of germ marked "Negaunee." It is possible that this is Eberth's germ, though of this I am not certain. Unless this be the exception, I have not found Eberth's germ in any of the waters.

The waters No. 140 to No. 147, inclusive, I have not been able to classify. When these samples were sent I preferred not to know the source of each water, and asked that they be designated by numbers. Since sending in my report I have twice written asking that I may be informed of the source of each water, but my request has not been answered. Omitting these samples, the remaining one hundred and forty samples are divided into the following classes, according to their supposed relation to typhoid fever. Thirty-three are placed in the first class, *i. e.*, they are waters which were believed to be causing typhoid fever at the time the samples were sent. Forty-four belong to the second class, *i. e.*, while typhoid fever is not prevailing among those who are using the water, the water is regarded as suspicious on account of the former existence of typhoid fever or on account of the unsanitary surroundings. Sixty-three belong to the third class. The first sixteen waters of first class I have elsewhere[1] discussed. In fifteen of these, germs toxicogenic to the lower animals were found.

No. 90 is the next belonging to this class: The city of Sault Ste. Marie takes its water supply above the rapids, and ordinarily it is a very pure water. In the fall of 1890, owing to a break in the lock, more than two hundred boats were detained for two days above the lock and in the immediate vicinity of the intake. Some ten days later typhoid fever appeared, and the deaths were reported to be not less than thirty. All the cases appeared within a few weeks, and sample No. 90 was taken at this time. After this first outbreak there were no new cases. Samples 103, 104, and 105 were collected about one month later, and while the disease was still prevailing, but at a time when no new cases were being reported. I have, therefore, placed them in the second class.

No. 92 furnishes a lesson of interest. Typhoid fever was confined to a certain portion of the city. The supply-pipe carrying water to this portion was, I am told, a wooden one. At one point of its course a privy vault had been dug down upon the pipe, and

[1] The Medical News, June 14, 1890.

had been used for some years. The wooden pipe, much decayed, was covered in the vault with fecal matter.

Dr. E. P. Christian, of Wyandotte, Mich., sent me samples Nos. 93 and 94, and along with these a sample of milk. The doctor had about thirty cases of continued fever, some of which he designated as typical and others as atypical typhoid. He soon ascertained that the families in which the typical cases existed took their milk from the same dairyman. No. 93 was taken from the well of the dairyman, and in both this and the milk I found bacillus venenosus. In the river water I found the liquefying toxicogenic bacillus. All who had the fever had used the river water, and some of those who drank both the milk and the river water had had the disease in an atypical form, but none of those who did not drink the milk had the typical form of the disease. These observations were reported to me by Dr. Christian after I sent him the report of the examination. My conclusions, as stated in the report, were as follows:

"I regard both the waters and the milk as unsafe. Of the two waters, that from the well is the worst, both chemically and bacteriologically. The milk was examined only bacteriologically. The poison-producing germ in the well water is identical with that in the milk. I am inclined to the opinion that if the typhoid fever is due to one of the waters, the well water is the one most likely to be the cause. Eberth's germ (the so-called typhoid fever germ) was not found in any of the samples. This, however, does not mean, in my opinion, that the waters would not cause typhoid fever. I have never yet found Eberth's germ in drinking-water (with one possible exception). The river water probably has changed in character since the sample was taken, but the well water certainly should not be used."

The men who had typhoid fever at Torch Lake worked in a saw mill, which was located on the bank of the lake. The well from which sample No. 95 was taken was at the mill, and near both well and lake was a large privy vault used by the men while at work. Sample No. 96 was taken from a well which was used by these men when not at work, and was more than a quarter of a mile from both well (No. 95) and lake. I knew nothing of these facts until some time after I had reported, as the samples when sent to me were distinguished by numbers.

In Nos. 101 and 102 I could find no toxicogenic germ, although it was believed that these waters were at the time causing typhoid fever. No. 102 was taken from a farmer's well, and one member of

the family after another came down with the fever. Whether there were other possible sources of infection about the place or not I do not know.

Sample No. 107 furnishes another illustration of my failure to find a toxicogenic germ in a water of the first class.

Nos. 109 and 110 were from wells from both of which the sick men had been accustomed to drink before coming down with the fever.

Nos. 111, 112, 113, and 114 came from the public water supply of Duluth, in January, 1891, during the prevalence of a very severe epidemic of typhoid fever. I found a toxicogenic germ in only one of the samples. This sample was taken, so the health officer informed me, from a tap in a doctor's office, the occupant of which had gone home some two weeks before with typhoid fever, and, so far as known, the tap had not been used since that time.

Samples of Drinking-Water Examined in the Hygienic Laboratory of Michigan University.

From October 1, 1888, to May 1, 1890.

No.	Water sent from	Source.	Class.	Free ammonia.	Albuminoid ammonia.	Chlorine.	Number of germs.	Kind of germ.	Remarks.
1	Omaha, Nebraska,	Well	Second	0.168	0.118	129.0	50		
2	" "	"	"	0.050	0.124	97.0	46	No. 13 was found in all the Omaha samples. No. 10 in samples No. 4. No. 1 in Nos. 1, 3, and 4. Nos. 11 and 12 in samples 5, 7, 8, 9, and 10. Undescribed germs were found in samples 2 and 4.	Pure cultures of each of these germs in beef-tea, twenty four hours old, were injected into the abdominal cavity of rabbits and rats. All were without effect.
3	" "	"	"	0.664	0.230	12.0	120		
4	" "	"	"	0.162	0.116	45.0	50		
5	" "	"	"	0.094	0.112	23.0	26		
6	" "	"	"	0.028	0.090	34.0	18		
7	" "	"	"	0.022	0.102	48.0	38		
8	" "	"	"	0.172	0.088	48.0	36		
9	" "	"	"	0.054	0.068	98.0	20		
10	" "	"	"	0.032	0.096	8.0	8		
11	Coldwater, Mich.	"	"	0.270	0.045	8.0	500		
12	" "	"	"	0.015	0.025	14.0	712	Nos. 10, 13, and 16 were found in these waters.	Inoculations of rabbits were without effect.
13	" "	"	"	0.270	0 040	15.0	370		
14	" "	"	"	0.025	0.040	12.0	580		
15	Ida, Mich.	"	"	0.910	0 120	155.0	2000	No. 13	Inoculation of rabbit was without effect.
16	Brown City, Mich.	"	"	0.220	0.096	8.0	400	Nos. 10 and 13.	Inoculations of rabbits were without effect.
17	Kalamazoo, Mich.	"	Third	0.041	0.084	7.0	63	Nos. 10 and 13	" " " " " "
18	" "	"	"	0.020	0.066	7.0	60		
19	Mount Pleasant, Mich.	River	Second	0.091	0.208	79.0	3000	Nos. 10 and 13	Inoculations of rats were without effect.
20	Gambier, Ohio,	Well	"	0.065	0.062	240.0	683	Nos. 1, 10, 11, 12, 13, and 16	Inoculations of all the germs on rats and rabbits were without effect.
21	Allegan, Mich.	"	"	0.206	0.148	33.0	300	No. 13.	Inoculation of rabbit was without effect.
22	Three Rivers, Mich.	"	Third	0.070	0.046	9.0	25		
23	" " "	"	"	0.108	0 072	7.0	20	No. 13	Inoculations of rats and rabbits were without effect.
24	" " "	"	"	0.024	0.054	7.0	22		
25	Allegan, Mich.	Hydrant	"	0.220	0.066	31.0	40	No. 13	Inoculations of rats were without effect.
26	" "	Artesian	"	0.272	0.556	32.0	25		
27	Coldwater, Mich.	Well	"	0.024	0.038	14.0	16	No. 13	Inoculation of rat was without effect.
28	Kalamazoo, Mich.	"	"	0.144	0.058	9.0	280	Nos. 10 and 13	Inoculations of rabbits were without effect.
29	Tecumseh, Mich.	"	Second	0.037	0.078	10 0	40	No. 13	Inoculation of rat was without effect.
30	Ishpeming, Mich.	Lake	Third	0.222	0.418	6.0	455		
31	" "	"	"	0.036	0.222	2.0	50	Nos. 10 and 13	Inoculations of rats and rabbits were without effect.
32	" "	"	"	0.038	0.208	3.0	48		
33	Three Rivers, Mich.	Well	"	0.200	0 036	0.9	30		
34	" " "	"	"	0.060	0.102	0.7	25	No. 13	Inoculations of rats were without effect
35	" " "	"	"	0.016	0.062	1.0	22		

36	St. Louis, Mich.	Reservoir	Third	0.060	0.210	23.0	8400	Nos. 10, 12, 13, 16, and 20	Inoculations of rats and rabbits were without effect.
37	" "	Pine River	"	0.044	0.320	24.0	1008	Nos. 10, 13, and 16	
38	Climax, Mich.	Well	Second	0.006	0.084	4.5	105	Nos. 10 and 13	Inoculations of rats were without effect.
39	Grand Rapids, Mich.	River	Third	0.030	0.134	10.0	36,000	Bacillus D.	Rabbits inoculated with No. 39 died, while those inoculated with No. 40 were not effected.
40	" " "	"	"	0.024	0.075	6.0	120		
41	Ann Arbor, Mich.	Cistern	First	2.223	0.908	3.0	3000	No. 29	Rats, guinea-pigs, and rabbits inoculated with [this germ died.
42	Negaunee, Mich.	Lake Teal	"	0.228	0.368	30.0	920	In No. 46, germs Nos. 1, 10, and 13 were found. In Nos. 42, 43, 44, and 45 there was found in addition to the above bacillus E.	Rabbits inoculated with bacillus E died; those inoculated with the other germs from the same waters were not affected.
43	" "	" "	"	0.232	0.460	30.0	1240		
44	" "	" "	"	0.296	0.448	10.0	772		
45	" "	Mine.	"	0.312	0.236	110.0	2050		
46	" "	Sand Shaft	Third	0.042	0.120	10.0	772		
47	Mendon, Mich.	Well	Second	0.019	0.048	4.0	25	No. 13	Rats were not affected.
48	" "	"	"	0.020	0.210	34.0	100	Nos. 1, 10, and 13	
49	Dearfield, Mich.	"	First	0.508	0.158	695.0	898	Bacillus C.	Rats inoculated with this germ died.
50	Northville, Mich.	"	Second	1.136	0.732	6.7	1550	No. 13	Inoculations of rats were without effect.
51	Iron Mountain, Mich.	"	First	1.256	1.920	44.0	1500		
52	" " "	"	"	0.384	0.840	20.0	1350		
53	" " "	"	"	0.781	0.960	52.0	1260	Nos. 13 and 31 were found in all these waters.	Rats, guinea-pigs, and rabbits inoculated with No. 31 died.
54	" " "	"	"	0.904	1.360	16.0	1700		
55	" " "	"	"	0.456	0.944	12.0	850		
56	" " "	"	"	0.464	1.256	28.0	950		
57	Ann Arbor, Mich.	Cistern.	"	0.318	0.262	6.0	1200	No. 29	Rats, guinea-pigs, and rabbits inoculated with No. 29 died.
58	" " "	"	"	0.492	0.504	9.0	1770		
59	Rankine, Illinois	Well	"	0.512	0.332	24.0	738	Nos. 13 and 31	No. 31 is fatal to rats, guinea-pigs, and rabbits.
60	Pomfret, Conn.	"	Second	0.104	0.116	4.0	351	Nos. 10 and 13	Inoculations of rats were without effect.
61	Sherwood, Mich	"	First	0.194	1.160	7.0	4116	No. 14	Rats inoculated with this germ were not affected.
62	Soudan, Minn.	Lake	Third	0.144	0.488	3.0	428	No. 11 and bacillus E.	Rats inoculated with E died.
63	" "	"	"	0.132	0.488	4.0	459	No. 11	Rats inoculated with No. 11 were not affected.
64	" "	Well	Second	0.120	0.090	2.0	28	No. 11	
65	" "	"	"	0.072	0.124	2.0	4	No. 29	Rats inoculated with No. 29 died.
66	Lake City, Mich.	Lake	Third	0.154	0.280	3.0	124	No. 11	Rats were inoculated without effect.
67	Iron Mountain, Mich	"	"	0.260	0.270	4.5	9	No. 11	" " " " " "
68	Ironwood, Mich.	Well	"	0.176	0.248	9.9	12	No. 11	" " " " " "
69	Ann Arbor, Mich.	Spring	"	0.012	0.016	2.5	0		
70	" " "	"	"	0.044	0.120	4.0	4	No. 11	" " " " " "
71	" " "	"	"	0.050	0.080	6.0	0		
72	" " "	"	"	0.090	0.214	4.0	6	No. 11	" " " " " "
73	Leslie, Mich.	Well	Second	0.536	0.840	14.0	104	Nos. 11 and 13	" " " " " "
74	" "	"	"	1.144	0.984	12.5	2940		
75	Ann Arbor, Mich.	"	Third	0.064	0.064	17.0	150	No. 14	" " " " " "
76	" " "	"	"	0.068	0.070	6.0	60	No. 14	" " " " " "
77	" " "	Spring	"	0.124	0.194	3.5	295	No. 11	" " " " " "

Samples of Drinking-Water Examined in the Hygienic Laboratory of Michigan University.

From May 1, 1890, to May 1, 1892.

No.	Water sent from	Source.	Class.	Free ammonia.	Albuminoid ammonia.	Chlorine.	Number of germs.	Kind of germs.	Remarks.
78	Three Rivers, Mich.	Well	Third	0.015	0.019	6.288	8 after 72 hours	No. 13	1 c.c. of beef-tea, twenty-four hours old, was injected into the abdominal cavity of rats without effect.
79	East Lake, Mich.	"	"	0.067	0.058	44.74	None	.....	60 drops of beef-tea, twenty-four hours old, were injected into the abdominal cavity of rabbit without effect.
80	Gladwin, Mich.	"	"	0.374	0.044	11.8	63 after 48 hours	Nos. 13 and 14	Inoculation of rat was without effect.
81	Alpena, Mich.	Hydrant	"	0.148	0.37	6.60	22 after 72 hours	Nos. 10 and 13	
82	" "	Spring	"	0.072	0.174	4.64	2880 after 72 hours	Nos. 10 and 13	Inoculations of rats were without effect.
83	Soudan, Minn.	Well	"	0.05	0.156	1.81	6 after 72 hours	No. 14	Inoculation of rat was without effect.
84	" "	"	"	0.058	0.132	2.14	3 after 72 hours	Nos. 10 and 13	Inoculations of rats were without effect.
85	" "	" (Artesian)	"	0.076	0.14	2.14	None	.....	Inoculation of rat without effect.
86	Gladwin, Mich.	"	"	0.26	0.102	1.32	10	Unknown	60 drops of beef-tea, twenty-four hours old, injected into abdominal cavity of guinea-pig. Animal died.
87	Imlay City, Mich.	"	"	0.52	0.052	1321.00	98 after 48 hours	Nos. 10 and 13 and unknown	1 drachm of beef-tea, twenty-four hours old, injected into abdominal cavity of a rat. Death in six hours
88	Gladwin, Mich.	"	"	0.526	0.116	21.45	12 after 72 hours	Nos. 10 and 13	20 drops of beef-tea culture, twenty-four years old, injected into abdominal cavity of rat. No effect.
89	Imlay City, Mich.	"	"	0.462	0.102	1328.25	None	.....	Inoculation of rat with negative results.
90	Sault St. Marie, Mich.	Lake	First	0.224	0.168	3.30	2000	No. 28	1 drachm of beef-tea, twenty-four hours old, injected into abdominal cavity of rat produced death.
91	Bay City, Mich.	Hydrant	Third	0.34	0.48	425.70	420	No. 10	Inoculation of rat produced no effect.
92	" " "	"	First	1.00	0.68	465.30	450	No. 31	20 drops of beef-tea, twenty-four hours old, injected into abdominal cavity of rat produced death.
93	Wyandotte, Mich.	Well	"	0.40	0.56	266.4	2430	Nos. 10 and 28	20 drops of beef-tea culture, twenty-four hours old, injected into abdominal cavity of rat produced death.
94	" "	River	"	0.08	0.52	49.5	1770	Nos. 10 and 31	20 drops of beef-tea culture, twenty-four hours old, injected into abdominal cavity of rat produced death.
95	Torch Lake, Mich	Lake	"	.....	.... .	.....	5284	Nos. 10 and 28	20 drops of beef-tea culture, twenty-four hours old, injected into abdominal cavity of rat caused death.
96	" " "	Well	"	.....	.....	.....	2520	No. 10	Inoculation of a rat produced no effect.

97	Torch Lake, Mich.	Well	First	.....	.....	.....	20	Nos. 10 and 28	Injection of 20 drops of beef-tea culture, twenty-four hours old, into peritoneal cavity killed rat.
98	Pontiac, Mich.	Hydrant	Second	0.422	0.574	9.9	23 after 48 hours	Nos. 10 and 13 and unknown	Inoculations of rats were without effect.
99	" "	Lake	"	0.266	0.302	9.075	18 after 48 hours	No. 10	Inoculation of rat was without effect.
100	" "	"	"	0.130	0.35	9.9	12 after 48 hours	No. 10	" " " " "
101	Negaunee, Mich.	"	First	0.024	0.820	6.105	10	No. 10	" " " " "
102	Parma, Mich	Well	"	0.058	0.124	100.65	1234	No. 10	" " " " "
103	Sault St. Marie, Mich.	Lake	Second	0.05	0.101	6.6	5	No. 4	" " " " "
104	" " "	"	"	0.06	0.12	8.25	12	No. 4	" " " " "
105	" " "	"	"	0.176	0.16	11.55	150	Nos. 10 and 4	Inoculations of rats were without effect.
106	Bay City, Mich.	Hydrant	Third	0.366	0.38	339.95	350	No. 10	Inoculation of rat was without effect.
107	Pontiac, Mich.	Well	First	0.198	0.368	14.55	240	No. 13	" " " " "
108	Three Rivers, Mich.	"	Third	0.172	0.212	9.90	26	Nos. 10 and 13	Inoculations of rats were without effect.
109	St. Johns, Mich.	"	First	0.094	0.13	18.15	11,025 after 48 hours	Nos. 13 and 28	1 c.c. of beef-tea culture, twenty-four hours old, was injected into the abdominal cavity of each of three rats, one died, two recovered.
110	" "	"	"	0.13	0.122	18.15	6	Nos. 10, 13, 4	Inoculations of rats were without effect.
111	Duluth, Minn.	Lake	"	0.04	0.124	7.2	200	No. 10	1 c.c. of a culture, forty-eight hours old, was injected into abdominal cavity of rat, results negative.
112	" "	"	"	0.058	0.12	8.25	198	No. 10	1 c.c. of a culture, forty-eight hours old, was injected into abdominal cavity of rat; result negative.
113	" "	"	"	0.007	0.264	8.25	20	Nos. 4, 10, 30	1 c.c of a culture, forty-eight hours old, was injected into abdominal cavity of rat; result death.
114	" "	"	"	0.038	0.058	9.075	1	No. 10	Inoculation of rat was without effect.
115	" "	Spring	Third	0.058	0.07	14.85	12 after 48 hours	No. 4	" " " " "
116	Leadville, Col.	From a mine	"	0.091	0.094	3.30	145 after 72 hours	Nos. 10 and 4	Inoculations of rats were without effect.
117	Iron Mountain, Mich.	Well	"	0.144	0.141	4.95	5	No. 10	" " " " "
118	" " "	Hydrant	"	0.57	0.57	4.95	6	No. 10	Inoculation of rat was without effect.
119	" " "	Lake	"	0.342	0.342	4.125	2	No. 10	" " " " "
120	" " "	"	Second	0.11	0.322	6.93	5	No. 10	" " " " "
121	" " "	"	"	0.092	0.311	7.09	4	No. 10	" " " " "
122	Gaylord, Mich.	Unknown	Third	0.39	0.98	26.40	670 after 48 hours	No. 13	Rats were inoculated without effect.
123	Iron Mountain, Mich.	"	Second	0.03	0.15	4.0	8	No. 13	Injection of 20 drops of beef-tea culture, twenty-four hours old, into abdominal cavity of a rat produced no effect.
124	Norway, Mich.	"	Third	0.01	0.03	1.0	6	Nos. 10 and 13	20 drops of beef-tea culture, twenty-four hours old, injected into the abdominal cavity of a rat produced no effect.
125	" "	"	"	0.02	0.15	3.0	10	Nos. 10 and 13	20 drops of beef-tea culture, twenty-four hours old, injected into the abdominal cavity of a rat produced no effect.
126	" "	Well	"	0.005	0.01	0.5	6	No. 13	Inoculation of rat was without effect.
127	Adrian, Mich.	Unknown	First	0.03	0.20	10.0	40 after 24 hours	Nos. 10 and 28	20 drops of beef-tea, twenty-four hours old, were injected into the abdominal cavity of a rat. Death resulted.

No.	Water sent from	Source	Class.	Free ammonia.	Albuminoid ammonia.	Chlorine.	Number of germs.	Kind of germs.	Remarks.
128	Iron Mountain, Mich.	Water works	Third	0.005	0.025	2.0	13 after 24 hours	Nos 10 and 21	Rats were inoculated without effect.
129	Pontiac, Mich.	Well	"	0.18	0.10	12.0	30 after 72 hours	Nos. 14 and 21	" " " " "
130	Ironwood, Mich.	River	Second	0.103	0.116	5.6	400 after 24 hours	Nos. 10, 12, 13	" " " " "
131	Iron Mountain, Mich.	Spring	Third	0.07	0.05	0.42	4	Nos. 10, 25, 26	" " " " "
132	Ithaca, Mich.	Unknown	"	0.41	0.15	25.0	500 after 24 hours	Unknown.	20 drops of beef-tea, twenty-four hours old, were injected into the abdominal cavity of a rat without effect.
133	Hastings, Mich.	Well	Second	0.20	0.11	18.0	850	Nos. 14 and 15	Rats were inoculated without effect.
134	Iron Mountain, Mich.	Lake	Third	0.15	0.08	1.3	4	Nos. 10 and 3	" " " " "
135	" " "	Spring	"	0.33	0.106	1.0	2	Nos. 10 and 3	" " " " "
136	Ithaca, Mich.	Well (deep)	"	0.302	0.24	2.8	None	.....	Rat was inoculated without effect.
137	Holland, Mich.	Water works.	Second	0.068	0.09	13.85	20	Nos. 13 and 14	Rats were inoculated with negative results.
138	" "	Well (deep)	"	0.514	0.166	15.675	180 after 48 hours	Nos. 13 and 14	" " " " " "
139	" "	Well (shallow)	"	0.088	0.134	6.93	120 after 48 hours	Nos. 13, 14, 20	" " " " " "
140	Chicago, Ill.	.....	.....	0.310	0.198	11.55	7	Nos. 9, 10, 24	" " " " " "
141	" "	.....	.....	0.042	0.06	10.395	90 after 48 hours	Nos. 17, 18, 23	" " " " " "
142	" "	.....	.....	0.31	0.148	11.85	4	Nos. 2 and 11	" " " " " "
143	" "	.....	.....	0.178	0.166	8.25	6	Nos. 7, 15, 26	" " " " " "
144	" "	.....	.....	0.44	0.196	10.98	9	Nos 3 and 27	" " " " " "
145	" "	.....	.....	0.176	0.106	13.20	48 after 48 hours	Nos. 2, 8, 9, 19, and 27	" " " " " "
146	" "	.....	.....	0.14	0.106	12.705	6	Nos. 2, 7, 10, 15, 19, 22	" " " " " "
147	" "	.....	.....	0.08	0.24	18.48	5	Nos. 6, 11, 13, 23	" " " " " "
148	Dunkirk, N. Y.	.....	Second	0.094	0.16	2.478	60 after 48 hours	Nos. 10 and 27	" " " " " "

Every now and then some one announces a new test, by means of which the Eberth germ can be distinguished from other germs in water. These announcements are founded upon comparisons with a few water germs, or with those which happen to exist in one or two samples of water. None of these tests have been systematically tried with a large number of germs. One of these tests, proposed by Parietti,[1] is made as follows: To 10 c.c. of neutral bouillon there is added from three to nine drops of the following solution:

Carbolic acid	5 grammes.
Pure hydrochloric acid	4 "
Distilled water	100 "

The tubes thus prepared are kept in the incubator for twenty-four hours at 37° C. in order to see that no contamination with germs from the air has occurred. To the tubes which remain clear, from one to ten drops of the suspected water is added, and the tubes returned to the incubator. If the beef-tea becomes cloudy within the next twenty-four hours, one can, according to Parietti, positively conclude that the typhoid germ is present. The excellence of this test has been attested by Kamen.[2]

Of the seven water germs described in the following tables as growing at 38°, every one grows abundantly in Parietti's solution. Of the twenty-four remaining germs, two were not tested and three were found to grow in Parietti's solution. These three are germs which grow feebly at 38° in ordinary beef-tea, and the addition of Parietti's solution did not further retard their growth.

Uffelmann[3] proposes a test by which many water germs can be excluded in searching for the Eberth germ. His medium consists of a citric acid gelatin, colored with methyl-violet. He states that only a small number of germs, other than the Eberth germ, will grow on this gelatin, and that these do not take up the coloring matter like the Eberth germ. Of the thirty-one water germs upon which I have made this test, nine grow, and some of these stain more intensely than Eberth's germ.

[1] "Metodo di ricerca del Bacillo del Tifo nelle acque potabili." Rivista d'Igiene e Sanità Publica, 1890.

[2] Centralblatt f. Bakteriolgie u. Parisitenkunde, B. xi., No. 2.

[3] Berliner klinische Wochenschrift, 1891, No. 35.

I have used the potato gelatin test of Holz,[1] with and without the addition of carbolic acid as is recommended, with all the toxicogenic germs described in this paper, and I find that all grow quite as readily and abundantly as the Eberth germ.

No. 1. *Micrococcus Candicans.*

Form. Large cocci often grouped in clusters, which vary much in size.
Growth:

On gelatin plates. Superficial colonies look like minute drops of milk. The deeper ones are more or less brown and granular.
In gelatin tubes. Grows along the line and forms a "nail head" on the surface.
On agar. A yellowish or brownish growth.
On potato. A white, slimy growth.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows at ordinary temperature, but not at 38°.
Rate of growth. Rapid.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. White.
Toxicogenic properties. Negative.

No. 2. *Micrococcus Aquatilis Albus.*

Form. Small cocci.
Growth:

On gelatin plates. Snow-white dots. Spherical colonies with many irregular forms.
In gelatin tubes. Very slight along the line, and spreading but little over the surface. The growth on the gelatin is not abundant.
On agar. Very slight, white growth.
On potato. Thick directly over the place of application, but spreading very little. The color is yellowish-white.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows slowly at ordinary temperature, and more feebly at 38° C.
Rate of growth. Very slow.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. White.
Toxicogenic properties. Negative.

[1] Zeitschrift f. Hygiene, B. viii., S. 143.

No. 3. *Micrococcus Aquatilis Magnus.*

Form. Very large micrococci.
Growth:
On gelatin plates. Deep brown colonies, with smooth outline.
In gelatin tubes. Few isolated colonies along the track. Spreads over the surface.
On agar. White, thin growth.
On potato. White or brownish granular growth.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows well at ordinary temperature, and feebly at 38° C.
Rate of growth. Moderate.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. White.
Toxicogenic properties. Negative.

No. 4. *Micrococcus Luteus.*

Form. Small micrococci, growing in zoöglea.
Growth:
On gelatin plates. Sulphur-yellow, granular colonies.
In gelatin tubes. Grows along the line and slowly spreads over the surface.
On agar. A lemon-yellow growth.
On potato. An abundant growth, which is at first dirty white, but which gradually becomes lemon-yellow.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows at ordinary temperature, but not at 38° C.
Rate of growth. Rapid.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. Lemon-yellow.
Toxicogenic properties. Negative.

No. 5. *Micrococcus Cereus.*

Form. Micrococci.
Growth:
On gelatin plates. Pale, yellow colonies, of smooth outline.
In gelatin tubes. Very slight along the track; spreads slowly over the surface.
On agar. Very faint, white growth.

On potato. Yellowish white, waxy growth. Beyond the border of the growth the potato becomes bluish gray.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows at ordinary temperature, but does not grow at 38° C.
Rate of growth. Slow.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. White to brownish-yellow.
Toxicogenic properties. Negative.

No. 6. *Micrococcus Subflavus.*

Form. Elliptical micrococci, growing in zoöglea.
Growth:
On gelatin plates. Yellowish-brown, spherical colonies.
In gelatin tubes. Very slight along the track; spreads slowly over the surface.
On agar. White to yellowish-white.
On potato. Pale, yellow growth, with sloping edges.
In Parietti's solution. Does grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows at ordinary temperature, and feebly at 38° C.
Rate of growth. Moderate.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. Pale yellow.
Toxicogenic properties. Negative.

No. 7. *Micrococcus Aquatilis Invisibilis.*

Form. Oval cocci.
Growth:
On gelatin plates. Deep brown colonies, with smooth outline; spreading irregularly superficially.
In gelatin tubes. Slight growth along the line, but spreading on the surface.
On agar. White, thin growth.
On potato. Invisible.
In Parietti's solution. Does grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows well at ordinary temperature, but feebly at 38° C.
Rate of growth. Slow.
Relation to air. Aërobic.

Production of gas. None observed.
Liquefaction. Negative.
Color. White.
Toxicogenic properties. Negative.

No. 8. *Diplococcus Aquatilis.*

Form. Diplococci.
Growth:
On gelatin plates. Smooth, pale yellow colonies, mostly spherical, but showing some irregularities.
On gelatin tubes. Growth confined to surface, where it spreads to the walls of the tube.
On agar. Smooth, white growth.
On potato. Dirty white and glazed; thick, with sloping borders.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Does not grow at 38°; grows well at ordinary temperature.
Rate of growth. Moderate.
Relation to air. Aërobic.
Production of gas. None.
Liquefaction. None.
Color. White.
Toxicogenic properties. Negative.

No. 9. *Streptococcus Aquatilis.*

Form. Large micrococci; some single, others in pairs, and some in chains of from four to eight.
Growth:
On gelatin plates. Colonies spherical, many having notched outlines.
In gelatin tubes. Grows very slightly along the line, but spreads over the surface to the walls of the tube.
On agar. Very thin, white growth.
On potato. Heavy, moist, white growth.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Does not grow at 38°; grows at ordinary temperature.
Rate of growth. Slow on gelatin; rapid on potato.
Relation to air. Aërobic.
Production of gas. None.
Liquefaction. Negative.
Color. White.
Toxicogenic properties. Negative.

No. 10. *Bacillus Fluorescens Liquefaciens.*[1]

Form. Very small bacilli; twice as long as broad.
Growth:
On gelatin plates. Small, round colonies, liquefying and sinking into the gelatin.
In gelatin tubes. Liquefies gelatin rapidly from surface evenly to bottom; no scum on surface; deposit heavy and yellowish white. The supernatant fluid is yellowish, with green fluorescence, most marked near the surface.
On agar. Thin white growth.
On potato. Smooth growth, with yellowish tint and sloping margins.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows at ordinary temperature, but does not grow at 38° C.
Rate of growth. Rapid at ordinary temperature.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Liquefies rapidly and completely.
Color. Yellowish white.
Toxicogenic properties. Negative.

No. 11. *Bacillus Fluorescens Non-liquefaciens.*

Form. Small bacilli, with rounded ends.
Motility. Non-motile.
Growth:
On gelatin plates. Glistening, mother-of-pearl colonies, spreading on the surface.
In gelatin tubes. Growth confined to surface, and dirty yellow in color; subjacent gelatin shows green fluorescence.
On agar. White on the surface, while the mass of agar becomes green.
On potato. Grayish white or brown growth, with glistening surface.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows well at ordinary temperature, but does not grow at 38° C.
Rate of growth. Rapid at ordinary temperature.

[1] I have found two varieties of this germ. The second differs from the one described in this table in the following particulars: 1. In gelatin tubes the liquefaction proceeds slowly, and after half or two-thirds of the gelatin has been liquefied, ceases altogether; the subjacent gelatin showing marked fluorescence. 2. It grows abundantly in Uffelmann's gelatin, and takes the stain more markedly than does Eberth's germ.

Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Non-liquefying.
Color. White, or yellowish to brownish white.
Toxicogenic properties. Negative.

No. 12. *Bacillus Gasoformans.*

Form. Small bacilli, two to three times as long as broad.
Motility. Motile.
Growth:
On gelatine plates. Large colonies, which rapidly liquefy the gelatin.
In gelatin tubes. Rapidly liquefies the gelatin, and bubbles of gas form along the line of inoculation.
On agar. A brownish or yellowish growth.
On potato. Dirty white growth.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows at ordinary temperature, but not at 38° C.
Rate of growth. Rapid.
Relation to air. Aërobic.
Production of gas. Produces gas abundantly.
Liquefaction. Liquefies gelatin rapidly.
Color. White.
Toxicogenic properties. Negative.

No. 13. *Bacillus Liquefaciens Albus.*

Form. Small rod, with rounded ends.
Motility. Very motile.
Growth:
On gelatin plates. Small, round colonies, liquefying rapidly.
In gelatin tubes. Grows rapidly, and completely liquefies the gelatin.
On agar. A dirty white growth.
On potato. Yellowish or brownish white.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Does not grow at 38°; grows well at ordinary temperature.
Rate of growth. Moderate.
Relation to air. Aërobic.
Production of gas. The gelatin tubes give off no odor, and for this reason this germ must not be confounded with the bacillus liquefaciens, as described by Eisenberg.
Liquefaction. Liquefies rapidly.
Color. White.
Toxicogenic properties. Negative.

No. 14. *Bacillus Albus.*

Form. Short bacilli, often in chains.
Motility. Motile.
Growth:
On gelatin plates. White, smooth colonies.
In gelatin tubes. Grows slowly along the line of inoculation, and forms a white "nail head" on the surface.
On agar. A milk-white growth.
On potato. A dirty yellowish-white growth.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Grows at ordinary temperature, but does not grow at 38° C.
Rate of growth. Slow.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Does not liquefy.
Color. White.
Toxicogenic properties. Negative.

No. 15. *Bacillus Albus Putridus.*

Form. Long and short bacilli, often growing in chains.
Motility. Motile.
Growth:
On gelatin plates. Round, white or brown colonies.
In gelatin tubes. Growth confined to surface, where it becomes very heavy. Liquefaction extends downward very slowly. (In these respects this germ differs from that described by Eisenberg under this name.) The contents of the tube give off a highly offensive odor.
On agar. Heavy, smooth growth.
On potato. Slimy, grayish-white; later, brownish growth.
In Parietti's solution. Does not grow.
In Uffelmann's gelatin. Does not grow.
Effect of temperature. Does not grow at 38°; grows well at ordinary temperature.
Rate of growth. Rapid.
Relation to air. Aërobic.
Production of gas. Gives off putrefactive odors.
Liquefaction. Liquefies slowly.
Color. White, or yellowish white.
Toxicogenic properties. Negative.

No. 16. *Bacillus Violaceus.*

Form. Bacilli about three times as long as broad, often growing in threads.

Motility. Motile.
Growth:

On gelatin plates. The colonies look like small air bubbles to the unaided eye. Under the microscope the colonies are granular and violet. Sometimes the surface of the gelatin is raised like a foam.

In gelatin tubes. Produces a funnel-shaped liquefaction, while the pale violet mass of germs lies at the bottom.

On agar. A blue to violet growth.

On potato. A dark violet growth.

In Parietti's solution. Not tested.

In Uffelmann's gelatin. Not tested.

Effect of temperature. Grows at ordinary temperature, but not at 38° C.
Rate of growth. Moderate.
Relation to air. Facultative anaërobic.
Production of gas. None observed.
Liquefaction. Liquefies.
Color. Produces a violet color.
Toxicogenic properties. Negative.

No. 17. *Bacillus Gracilis Aërobiens.*

Form. Bacilli four to six times as long as broad.
Motility. Motile.
Growth:

On gelatin plates. Small, yellow colonies of rapid growth.

In gelatin tubes. Grows abundantly along the track.

On agar. Grayish-white, feeble growth.

On potato. A waxy growth of pinkish-white color, while beyond the growth the potato becomes steel gray.

In Parietti's solution. Does not grow.

In Uffelmann's gelatin. Grows abundantly, and stains more intensely than does Eberth's germ.

Effect of temperature. Grows at ordinary temperature; does not grow at 38°.
Rate of growth. Rapid.
Relation to air. Aërobic.
Production of gas. None observed.
Liquefaction. Negative.
Color. White to gray.
Toxicogenic properties. Negative.

No. 18. *Bacillus Gracilis Anaërobiescens.*

Form. Bacilli three times as long as broad, often growing in long, slender rods.
Motility. Very motile.

Growth:

On gelatin plates. Brownish colonies, spreading irregularly.

In gelatin tubes. Grows abundantly along the line, and also spreads over the surface.

On agar. Thin, white growth.

On potato. Growth is yellowish white, abundant and prominent. Stains made from potato show long threads, with shorter bacilli near, often presenting the appearance of fringe.

In Parietti's solution. Grows.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows well at ordinary temperature, and feebly at 38°.

Rate of growth. Rapid.

Relation to air. Grows under gelatin.

Production of gas. Forms gas abundantly when grown under gelatin.

Liquefaction. Negative.

Color. White.

Toxicogenic properties. Negative.

No. 19. *Bacillus Helvolus.*

Form. Short bacilli, often growing in chains, and frequently forming long threads.

Motility. Only an oscillation.

Growth:

On gelatin plates. Small, yellowish or brownish colonies.

In gelatin tubes. Forms on the surface a spreading white growth, which later becomes yellow. The growth spreads to the walls of the tube, and very slowly sinks in the gelatine as liquefaction goes on. The growth along the line is very slight, or wanting altogether.

On agar. Yellowish white growth.

On potato. Yellow.

In Parietti's solution. Does not grow.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows well at ordinary temperature, but only feebly at 38°.

Rate of growth. Slow.

Relation to air. Aërobic.

Production of gas. None observed.

Liquefaction. Liquefies very slowly.

Color. White to yellow.

Toxicogenic properties. Negative.

No. 20. *Bacillus Rubidus.*

Form. A bacillus four to six times as long as broad.

Motility. Sluggishly motile.

Growth:

On gelatin plates. Yellowish, irregular colonies.

In gelatin tubes. Slight growth of isolated colonies along the line; these soon become pink in color. The growth at the surface is abundant, and as the gelatin liquefies large masses of the germ, with faint pink tint along the lower border, float in the liquid.

On agar. Faint yellowish growth, with no evidence of the possible development of color shown on some other media.

On potato. The growth has at first a slight pinkish tint, which, with age, develops into a beautiful red.

In Parietti's solution. Does not grow.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows well at ordinary temperature, but does not grow at 38° C.

Rate of growth. Moderate.

Relation to air. Aërobic.

Production of gas. None observed.

Liquefaction. Liquefies slowly.

Color. Red.

Toxicogenic properties. Negative.

No. 21. *Bacillus Cinnabareus.*

Form. A short bacillus.

Motility. Highly motile.

Growth:

On gelatin plates. Brick-red colonies.

In gelatin tubes. Liquefies rapidly and completely.

On agar. Cinnabar-red growth.

On potato. An abundant growth, at first yellowish-white, becoming more red with age.

In Parietti's solution. Not tested.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows at ordinary temperature; does not grow at 38° C.

Rate of growth. Rapid.

Relation to air. Not tested.

Production of gas. None observed.

Liquefaction. Liquefies rapidly.

Color. Cinnabar-red.

Toxicogenic properties. Negative.

No. 22. *Bacillus Subflavus.*

Form. Bacilli two to three times as long as broad.

Motility. Motile.

Growth:

On gelatin plates. Small, glistening, white, irregular colonies.

On gelatin tubes. Grows but slightly along the track; spreads over the surface. The tube shows slight fluorescence.

On agar. Yellowish-white growth; with age the mass of agar becomes brownish-yellow.

On potato. A beautiful salmon-colored granular growth.

In Parietti's solution. Does not grow.

In Uffelmann's gelatin. Grows abundantly, and stains more intensely than Eberth's germ.

Effect of temperature. Grows at ordinary temperature; does not grow at 38° C.

Rate of growth. Rapid.

Relation to air. Aërobic.

Production of gas. None observed.

Liquefaction. Negative.

Color. Yellowish-white.

Toxicogenic properties. Negative.

No. 23. *Bacillus Ochraceus.*

Form. Bacilli two to three times as long as broad, with rounded ends.

Motility. Non-motile. (In which respect it differs from Zimmermann's germ of the same name.)

Growth:

On gelatin plates. Small, yellow, irregular colonies, spreading slightly over the surface.

In gelatin tubes. Slowly liquefies evenly from the surface; the mass of germ lying on the bottom of the liquefied part, and showing at first a pale yellow, then an orange growth.

On agar. Forms an even yellow growth.

On potato. A beautiful and abundant growth of ochre yellow. This growth is very thick and heavy, and in this respect differs from the germ of Zimmermann.

In Parietti's solution. Does not grow.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Does not grow at 38°; grows well at ordinary temperature.

Rate of growth. Moderate.

Relation to air. Aërobic.

Production of gas. None.

Liquefaction. Liquefies slowly.

Color. Orange to ochre.

Toxicogenic properties. Negative.

No. 24. *Bacillus Figurans.*

Form. Bacilli two to three times as long as broad, but showing marked variation in form. Sometimes they appear as very short bacilli, while at other times they grow into long threads.

Motility. Sluggishly motile.

Growth:

On gelatin plates. The deep colonies are spherical and smooth, but the superficial growth forms curved and interlacing lines, often presenting most grotesque figures. Plates may show no liquefaction after some days.

In gelatin tubes. Does not develop along the line. Generally liquefies from the surface before the growth has reached the walls of the tube. Liquefaction, however, goes on very slowly, and, in some instances, the fluid is lost by evaporation as fast as it liquefies, and consequently there is apparently no liquefaction. After the gelatin has been liquefied half way down the tube, the mass of germs subsides, and further liquefaction is very slow or does not occur at all.

On agar. Forms a thin white growth, with heavy deposit often in water of condensation.

On potato. Abundant, faintly yellow, mucilaginous growth, without raised edges.

In Parietti's solution. Does not grow.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows well at ordinary temperature; feebly at 38° C.

Rate of growth. Very rapid at ordinary temperature.

Production of gas. None observed.

Liquefaction. Liquefies half-way down the tube.

Color. White.

Toxicogenic properties. Negative.

No. 25. *Micrococcus Aquatilis.*

Form. Small cocci, often in groups.

Growth:

On gelatin plates. Small, round, white colonies.

In gelatin tubes. Very feeble growth along the line, but spreading over the surface.

On agar. White, thin growth.

On potato. Brownish, moist growth.

In Parietti's solution. Grows.

In Uffelmann's gelatin. Does not grow.

Effect of temperature. Grows at ordinary temperature, also at 38° C.

Rate of growth. Slow.

Relation to air. Aërobic.

Production of gas. None observed.

Liquefaction. Negative.
Color. White.
Toxicogenic properties. Negative.

No. 26. *Bacillus Albus Anaërobiescens.*

Form. Bacilli, two to three times as long as broad.
Motility. Only an oscillation.
Growth:

On gelatin plates. Smooth, spherical, yellowish or brownish colonies.

In gelatin tubes. Grows well along the track, and spreads over the surface.

On agar. Heavy, milk-white growth.

On potato. Yellowish-white, glistening growth.

In Parietti's solution. Grows.

In Uffelmann's gelatine. Grows, and stains with the same intensity as Eberth's germ.

Effect of temperature. Grows at ordinary temperature, and also at 38° C.
Rate of growth. Rapid.
Relation to air. Grows under gelatin.
Production of gas. None observed.
Liquefaction. Does not liquefy.
Color. White.
Toxicogenic properties. Negative.

No. 27. *Bacillus Invisibilis.*

Form. Large bacilli, from two to five times as long as broad, with rounded ends.
Motility. Motile.
Growth:

On gelatin plates. Pale yellow burr-like colonies, with irregular outline, and spreading slightly.

In gelatin tubes. Grows abundantly along the track, and spreads slowly over the surface.

On agar. Thick white growth, with but little tendency to spread.

On potato. Invisible growth.

In Parietti's solution. Grows.

In Uffelmann's gelatin. Grows abundantly, but does not take up the stain.

Effect of temperature. Grows at ordinary temperature, and at 38°.
Rate of growth. Rapid.
Relation to air. Grows under gelatin.
Production of gas. None observed.
Liquefaction. Does not liquefy.
Color. White.
Toxicogenic properties. Negative.

No. 28. *Bacillus Venenosus.*

Form. A bacillus from two to four times as long as broad, with rounded ends.

Motility. Very motile.

Growth:

On gelatin plates. Small, white dots, spherical, and sometimes slightly yellow. The superficial colonies are raised above the surface of the gelatin.

In gelatin tubes. Grows abundantly along the line, and slowly spreads over the surface. When taken from the spleen of an animal which has died twelve days or later after inoculation, the tendency to spread over the surface of the gelatin is less marked than with the germ which has not passed through the animal body.

On agar. A thin white growth.

On potato. A light brown, moist growth. When the germ is taken from the spleen of an inoculated animal the growth is often invisible.

In Parietti's solution. Grows abundantly.

In Uffelmann's gelatin. Grows abundantly, and the superficial colonies stain intensely, while the deeper ones are not so markedly stained as those of the Eberth germ.

Effect of temperature. Grows rapidly both at ordinary temperature and at 38° C.

Rate of growth. Rapid.

Relation to air. Grows well under gelatin.

Production of gas. None observed.

Liquefaction. Does not liquefy.

Color. White.

Toxicogenic properties. Toxicogenic in rats, mice, guinea pigs, and rabbits. See experimental evidence on this point given later.

No. 29. *Bacillus Venenosus Brevis.*

Form. A thick, short bacillus; length about twice the width; grows in threads in old cultures.

Motility. Motile.

Growth:

On gelatin plates. Small, round colonies, with concentric rings. Generally, the deeper colonies are yellowish or brown. The surface colonies are raised, and spread but little. On plates made from the spleen of an inoculated animal the colonies are less regular in outline, and show a marked tendency to spread over the surface.

In gelatin tubes. Grows well along the line and spreads slowly over the surface, but finally extends to the sides of the tube.

On agar. Thin, white growth.

On potato. Moist, light brown, thick growth. Cultures which have been kept for fourteen days or longer at 40° form an invisible growth on potato. The medium used in these experiments was fresh spleen from man.

In Parietti's solution. Grows abundantly.

In Uffelmann's gelatin. Grows slowly, and takes the stain less markedly than does Eberth's germ.

Effect of temperature. Grows both at ordinary temperature and at 38° C.

Rate of growth. Rapid.

Relation to air. Grows well under gelatin.

Production of gas. None observed.

Liquefaction. Does not liquefy.

Color. White.

Toxicogenic properties. Toxicogenic in rats, mice, and guinea-pigs, and rabbits.

No. 30. *Bacillus Venenosus Invisibilis.*

Form. A slender bacillus; length, from two to four times the breadth. Ends are rounded.

Motility. Motile.

Growth:

On gelatin plates. Colonies are small, yellowish, and granular. Surface colonies are very irregular in shape and size, and are coarsely granular.

In gelatin tubes. Grows very slowly both along the line and at the surface; scarcely visible after three days.

On agar. A very thin, white growth.

On potato. On some potatoes the growth is invisible; on others there is a light brown growth.

In Parietti's solution. Grows well.

In Uffelmann's gelatin. Grows well and stains.

Effect of temperature. Grows at ordinary temperature and at 38°.

Rate of growth. Slow.

Production of gas. None observed.

Liquefaction. Does not liquefy.

Color. White.

Toxicogenic properties. Toxicogenic, but in less degree than bacillus venenosus. (See inoculation experiments.)

No. 31. *Bacillus Venenosus Liquefaciens.*

Form. A bacillus, whose length is from one and one-half to two times its breadth, and which has rounded ends.

Motility. Motile.

Growth:

On gelatin plates. The superficial colonies are raised, and spread over the surface. The deep colonies are yellowish and finely granular, with unbroken outline.

In gelatin tubes. Grows along the line abundantly, and spreads over the surface slowly. Liquefaction begins after from four to six weeks.

On agar. A thin, white growth.

On potato. A moist, light brown or yellowish growth. When kept for fourteen days or longer on spleen tissue, it forms an invisible growth on potato.

In Parietti's solution. Grows abundantly.

In Uffelmann's gelatin. Grows abundantly and stains deeply.

Effect of temperature. Grows at ordinary temperature and at 38°.

Rate of growth. Rapid.

Relation to air. Grows under gelatin.

Production of gas. Gas bubbles occasionally appear in gelatin tubes.

Liquefaction. Liquefies gelatin after some weeks.

Color. White.

Toxicogenic properties. Toxicogenic to mice, rats, guinea-pigs, and rabbits. (See inoculation experiments.)

The effects of the toxicogenic germs which I have described are compared with those of the Koch-Eberth germ. None of these can be said to be highly toxicogenic to the lower animals. They are not comparable with the germs of anthrax, glanders, tetanus, or diphtheria. I have made a great many inoculation experiments with these germs, but will detail only a few which I have made recently. In my inoculation experiments with Eberth's bacillus I have used a germ obtained by myself from the spleen of a person dead from typhoid fever, and a germ obtained from the Berlin Hygienic Laboratory. The two sets of inoculation are detailed separately.

Results of Inoculations.

bacillus venenosus.

Experiments 1–5.—Five white rats were inoculated by the injection of two cubic centimetres of an alkaline nuclein[1] culture, twenty-six days old, into the abdominal cavity. All died within twenty-four hours. The spleen, kidneys, and liver were found engorged. Plates made from these organs showed abundant growth of the germ in pure culture. Five cubic centimetres of this culture, after being freed from germs by filtration through porcelain, were injected into the abdominal cavities of rats without effect.

[1] The preparation of this medium will be described in a later paper on the chemical products of these germs.

Exp. 6–20.—Fifteen white rats were inoculated by the injection of two cubic centimetres of a beef-tea culture, grown for twenty-four hours at a temperature of 38°, into the abdominal cavity. All died within twenty-four hours. The spleen, kidneys, and liver were engorged. Plates made from these organs gave positive results.

Exp. 21–26.—Five white rats were inoculated by the injection into the abdominal cavity of one cubic centimetre of a beef-tea culture, grown for twenty-four hours at 38°. All died within twenty-four hours. Results of the examination and of the plates were the same as those given above. Six cubic centimetres of this culture, after being freed from germs by filtration through porcelain, were injected into the abdominal cavity of rats without effect.

Exp. 27–29.—Three white mice were inoculated by the subcutaneous injection of one cubic centimetre each of nuclein culture six days old. The inoculations were made at 4 P. M. Up to 9 P. M. the animals were apparently unaffected. The next morning they were found with eyes closed, rough coat, refusing to eat, and lying in a stupid state. They remained in this condition throughout the day, and were found dead the next morning, about forty hours after being inoculated. All of these mice suffered from diarrhœa before death. Post-mortem examination showed the intestines containing yellowish, watery feces. No marked changes were observed. Plates were made from the spleen, kidney, and liver of each. All these plates showed pure cultures of the germ.

Exp. 30. A guinea-pig was given two cubic centimetres of a nuclein culture six days old, under the skin of the back. The animal died after forty-eight hours. Examination showed the spleen slightly enlarged, and the intestines filled with watery feces. The animal had marked diarrhœa the day before it died. Plates were made from the spleen, tube cultures from the plates, and potato cultures from the tube. The growths on the potatoes were all less marked than those on companion potatoes made from the tubes of the germ which had not been through an animal.

Exp. 31–33.—Three white rats were given each one cubic centimetre of nuclein culture, six days old, under the skin of the back. The next day all had rough coats and all refused to eat. On the third day after the inoculation one of the rats died. Post-mortem showed the intestines inflamed, and the surface of the liver marked with many white nodules, each of which was about an eighth of an inch in diameter. These spots contained pure cultures of the germ. The spleen, which was engorged, also yielded the germ in large numbers. One of the rats seemed to gradually improve and on the twentieth day it was killed and the kidney, spleen, and liver plated. These plates remained sterile. The third rat developed three large, lymphatic tumors, one in each groin and one in the left axilla. The animal ate its food but still retained its rough coat and became very much emaciated. On the thirtieth day after the inoculation the animal was killed and plates were made from one of these tumors and from the liver, spleen, and kidney. The only abnormality observed in the abdominal organs was the enlargement of

the spleen, which was twice as large as normal. A small number of colonies appeared on the plates made from the spleen, while the other plates remained sterile. Tubes were made from the spleen plates and the identity of the germ fully determined. This shows that this bacillus may live in the body of the rat for thirty days. This result I regard as exceptional, and due to the condition of the animal more than to the virulence of the germ.

Exp. 34 and 35.—Injected under the skin of the back of each of two gray mice one cubic centimetre of a twenty-four hours' beef-tea culture. The next day these animals remained in a lethargic condition, and on the following day they died. There was marked congestion of the bloodvessels of the mesentery and, in one, fecal matter was found in the peritoneal cavity. The spleen, liver, and kidney were dark. Plates made from these organs developed the germ.

Exp. 36 and 37.—Injected under the skin of the back of each of two guinea-pigs two cubic centimetres of a twenty-four hours' beef-tea culture; both had rough coats and ate but little during the next two days. After this one rapidly improved and was soon apparently well. The other gradually lost flesh and died on the twelfth day after inoculation. The only abnormality which could be detected was an enlargement of the spleen, which was at least four times the size of this organ in healthy guinea-pigs. From the spleen, liver, and kidney cultures were made, and on each plate a small number of colonies of the germ appeared. Tube and potato cultures were made from these plates, and a wholly invisible growth formed on the potatoes.

Exp. 38–40.—Inoculated three white rabbits by the injection of three cubic centimetres of an alkaline nuclein culture under the skin of the back. Two of the animals were, so far as could be seen, not affected. The third began, on the second day, to show evidence of a profuse diarrhœa, which continued and was accompanied by great emaciation. The animal continued to eat, and, indeed, it ate more than either of the others, and seemed to have an insatiable appetite. The diarrhœa and emaciation continued for two weeks, and at the expiration of this time it was much reduced, but it continued to eat and soon began to regain flesh. After two weeks more it showed but slight evidence of the previous emaciation.

Exp. 41.—Injected two cubic centimetres of a nuclein culture into the abdominal cavity of a white rabbit about eight weeks old. The next morning the animal had a profuse diarrhœa, and died within forty-eight hours after the inoculation. The spleen was much congested and the small intestines highly inflamed. Plates made from the spleen, liver, and kidney showed abundant germs.

Exp. 42.—Injected two and one-half cubic centimetres of beef-tea culture, seven days old, under the skin on the back of a guinea-pig which had survived a previous inoculation with Eberth's germ. The animal was not affected, so far as could be seen.

BACILLUS VENENOSUS BREVIS.

Exp. 1 and 2.—Injected three cubic centimetres of a beef-tea culture, twenty-four hours old, into the abdominal cavity of each of two large rabbits. Both animals died within thirty hours. The spleen, liver, and mesentery were much congested. Cultures made from the spleen, liver, and kidney showed numerous colonies of the germ.

Exp. 3.—Injected two cubic centimetres of a beef-tea culture into the abdominal cavity of a large rabbit. The animal died within twenty-four hours. The post-mortem appearance and the cultures corresponded with those in the preceding experiments.

Exp. 4.—Injected one and one-half cubic centimetres of a beef-tea culture, twenty-four hours old, into the peritoneal cavity of a large rabbit. The animal rapidly emaciated, and the temperature in the rectum was taken twice a day from the eighth to the seventeenth day after inoculation, and was found to vary from 103° to 104.4°. During this time there was profuse diarrhœa. On the eighteenth day the animal was so weak that it could not stand and it was chloroformed and examined. The following observations made at the examination are given:

1. There was no evidence of suppuration at the point of inoculation or elsewhere.
2. The lower four inches of the small intestines were dark and congested externally, and the lower two inches were entirely denuded of epithelium.
3. The intestines contained a yellowish, frothy fluid.
4. The spleen, liver, and kidney were enlarged and somewhat hardened.
5. Cultures from these organs gave pure cultures of the germ.

Exp. 5.—Fifteen drops of a beef-tea culture were injected into the abdominal cavity of a rat; the animal was found dead the next morning. The spleen, liver, and kidney were congested and cultures from these organs gave positive results.

Exp. 6–10.—Two cubic centimetres of a beef-tea culture were injected under the skin on the back of each of five guinea-pigs. All died within from two to ten days after the inoculation. In all the spleen was found enlarged and cultures from this organ gave positive results

Exp. 11 and 12.—One cubic centimetre of a beef-tea culture was injected under the skin on the back of each of two white mice; the animals died within forty-eight hours and cultures from spleen, liver, and kidney showed abundant colonies of the germ.

BACILLUS VENENOSUS INVISIBILIS.

Exp. 1–10.—Injected one cubic centimetre of a beef-tea culture into the abdominal cavity of each of ten white rats. All died within forty-hours. The spleen, liver, and kidney were congested and cultures from these organs gave positive results.

Exp. 11–14.—Injected one cubic centimetre of a beef-tea culture, twenty-four hours old, under the skin of the back of each of four white mice. All

died on the second day. Cultures from the spleen, liver, and kidney gave positive results.

Exp. 15 and 16.—Injected one and one-half cubic centimetres of a nuclein culture under the skin on the back of each of two guinea-pigs; the animals were not affected.

Exp. 17.—Injected one cubic centimetre of a beef-tea culture under the skin on the back of gray mouse. The animal died within twelve hours and cultures were made from the spleen, liver, and kidney with positive results.

BACILLUS VENENOSUS LIQUEFACIENS.

Exp. 1–3.—Injected one cubic centimetre of a beef-tea culture, twenty-four hours old, under the skin on the back of each of three gray mice. One died within eighteen hours, a second within thirty hours, and the fourth within forty-eight hours. Post-mortem examination in each showed marked engorgement of the mesentery and the spleen. Plates revealed the presence of the germ.

Exp. 4–12.—Injected fifteen drops of a beef-tea culture into the abdominal cavity of each of ten white rats. All died within twenty-four hours. Examinations showed the spleen markedly engorged and the liver and kidney slightly so. Plates from these organs gave positive results. Five cubic centimetres of this culture, after filtration through porcelain, were injected into the abdominal cavity of each of five rats without causing death.

Exp. 13.—Injected three cubic centimetres of a beef-tea culture, seventy-two hours old, into the abdominal cavity of a rabbit. The animal died within twenty-four hours. The spleen was found engorged and cultures showed the presence of the germ.

EBERTH'S GERM (*from spleen*).

Exp. 1.—Injected three cubic centimetres of a beef-tea culture, twenty-four hours old, into the abdominal cavity of a rabbit. The animal died within twenty-four hours.

Exp. 2.—Same as No. 1, except that the animal remained apparently unaffected until the eleventh day, when it was found to be completely paralyzed in the posterior extremities. Two days later the rabbit died. Examination showed the mesenteric glands very much enlarged. The mucous membrane of the small intestine was congested; Peyer's patches enlarged; externally the lower end of the small intestine was covered with a plastic exudate. Cultures were made from kidney, liver, spleen, and blood, but all the plates remained sterile.

Exp. 3–5.—Injected one cubic centimetre of a beef-tea culture, twenty-four hours old, into the abdominal cavity of each of three white rats. One died after forty hours. The mucous membrane of the lower portion of the small intestine was markedly inflamed. Cultures gave positive results. The other rats were not seriously affected.

Exp. 6–8.—Injected into the abdominal cavity of three white rats, respec-

tively, fifteen, ten, and five drops of a beef-tea culture, twenty-four hours old. The one which had ten drops died within twenty-four hours. The post-mortem appearances were like those of the rat which had one cubic centimetre. The other rats were not affected.

Exp. 9–11.—Injected two cubic centimetres of a beef-tea culture into the abdominal cavity of each of three white rats. Two died within twenty-four hours, in each the lower portion of the small intestine was inflamed internally and covered with a plastic exudate externally. Plates made from the liver, spleen, and kidney, gave positive results. The third rat recovered.

Exp. 12.—Injected one-half cubic centimetre into the abdominal cavity of a white rat. The animal did not appear to be seriously affected. It was killed on the fourth day. The spleen was about three times the normal size. Cultures gave numerous colonies.

Exp. 13.—Injected one cubic centimetre of a beef-tea culture, twenty-four hours old, into the abdominal cavity of a half-grown rabbit. The animal died within twenty-six hours. The mucous membrane of the lower portion of the small intestine was slightly inflamed. No other changes were observed. Plates showed numerous colonies.

Exp. 14.—Injected into the abdominal cavity of a guinea-pig one cubic centimetre of a beef-tea culture, twenty-four hours old. The animal died within twenty-four hours. There was slight redness of the small intestine. Cultures gave positive results.

EBERTH'S BACILLUS (*from Berlin*).

Exp. 1 and 2.—Injected one cubic centimetre of a beef-tea culture, twenty-four hours old, into the abdominal cavity of each of two white rats. One died within twenty-four hours. The lower portion of the small intestine was inflamed, and was covered externally with a plastic exudate. The second rat did not die, but was killed on the fourth day. The spleen was enlarged, but not so markedly as in the rat which had been inoculated with the bacillus from the spleen.

Exp. 3 and 4.—Injected two cubic centimetres of a beef-tea culture, twenty-four hours old, into the abdominal cavity of each of two white rats. One died within twelve hours. The spleen, liver, and kidney were engorged. Plates were successful. The second rat did not appear to be affected by the inoculation.

Relation of these Toxicogenic Germs to the Bacillus of Eberth.

From the studies which I have detailed the following points seem to me to be demonstrated :

1. In their effects upon the lower animals these toxicogenic germs are fully equal in virulence to the Eberth bacillus.

2. The post-mortem appearances in animals dying after inocula-

tion with these germs are practically identical with those observed in animals killed by inoculation with the Eberth germ.

3. While the bacillus venenosus, as taken from water, forms on potatoes a growth wholly different from that of the Eberth bacillus, the former, when taken from animals which have survived the inoculation for twelve days or longer, forms on the potato the invisible growth which is generally supposed by bacteriologists to be characteristic of the Eberth bacillus.

4. Two of these toxicogenic germs form on potatoes invisible growths, when taken from cultures in human spleen which have been kept at a fever temperature for some days.

5. The fourth toxicogenic germ, when taken directly from the water, forms an invisible growth on potatoes.

If we add to these the fact well known to bacteriologists, that there are marked morphological and culture differences between Eberth germs from spleens in different epidemics of typhoid fever, and that the most skilful bacteriologists have reported most diversely upon the reaction of the Eberth germ with staining reagents, the evidence becomes sufficient to convince me that the Eberth germ, as found in the spleens and other organs after death, is not a specific microörganism, but is a modified or involution form of any one of a number of related germs. (I have refrained from discussing the reaction of these germs with staining reagents in this paper, because I have elsewhere gone quite thoroughly into this point of controversy.)

If we cannot agree in this conclusion we must accept the view of Babes, that there are varieties of the Eberth bacillus. It probably makes but little difference whether we conclude that these germs are varieties of one species or that they are related species. I know of no hard and fast lines upon which one can decide, to the satisfaction of everyone else, whether two or more germs, differing more or less, should be classified as species or as varieties. Of one thing I am certain, and that is that I am ignorant of any crucial test, or of any combination of tests, upon the strength of which I can say at present that a germ which I may find in drinking-water is identical with the so-called typhoid bacillus. I have found in spleens after death from typhoid fever, germs which differ from the typhoid bacillus obtained from Berlin, and from one another as markedly as my bacillus venenosus differs from either or both.

DISCUSSION.

DR. G. M. STERNBERG: I would like to ask whether these toxicogenic germs resemble the typhoid bacillus in morphology, and whether they belong to the same class or group.

DR. VAUGHAN: The germs are all bacilli and all motile. One I have called the bacillus venenosus. It is very much like Eberth's germ—that is, some of the Eberth's germs that I have obtained; I find a great difference in Eberth's germs—what I get from one spleen differs from that taken from another. It is shorter and thicker than the Eberth germ that I got from the Hygienic Institute at Berlin. Another bacillus, the bacillus venenosus brevis, is still shorter; it is about twice as long as broad. It grows in very much the same way. There is one that liquefies gelatin, but only after four to six weeks. After it has been grown at a high temperature, 40°, for a while, it ceases to liquefy gelatin.

DR. STERNBERG: It is interesting that this germ liquefies at one time, and at another time does not. It is only one case out of a good number that have been noticed by bacteriologists. For instance, some of the phosphorescent bacteria that liquefy at first, after a time fail to liquefy. I got out a bacillus in Cuba which was a liquefying bacillus for a time, and after a time it failed to liquefy. We cannot, therefore, use the liquefaction of gelatin as an absolute characteristic to enable us to differentiate these bacteria. Just as we have differences in pathogenic power, so we have, under artificial conditions, in our culture media, differences in the power to produce the ferment which causes liquefaction. So that, in the differentiation of these bacteria, Dr. Vaughan has found, as many others have found, a very great difficulty in deciding the question as to whether we have simply different varieties or well-defined species. There can be no doubt that we have species as well defined as in the higher plants. The definite characters which were first given to the typhoid bacillus will not stand. As to the invisible growth upon potato, we have all given that up as being distinctive. Other bacteria, as I think Dr. Welch has observed, have an invisible growth, and the typhoid bacillus does not always have an invisible growth. Under some circumstances you may get quite a visible moist film on the surface of the potato. It depends on the reaction of the potato, perhaps, and the difference in variety. There are many varieties without doubt. I simply want to call attention to the very great difficulty we encounter in differentiating these lower organisms.

DR. W. H. WELCH: There are one or two points in Dr. Vaughan's paper not quite clear to my mind. The first regards his distinction between the terms pathogenic and toxicogenic. The distinction is not what I anticipated it would be. I supposed that he would designate as a toxicogenic germ one

that causes death by intoxication without multiplication of the germs inside the body. The distinction which he makes is doubtful and is difficult to carry out practically. Toxicogenic and pathogenic germs, according to Dr. Vaughan, are both capable of multiplication within the body, but the pathogenic ones cause lesions and symptoms that are definite and recognizable, and the toxicogenic ones cause symptoms and lesions that are vague and undefined. It seems to me this distinction is indefinite and of little value. I agree with Dr. Vaughan as regards the difficulty in the recognition of the Eberth bacillus. It is very difficult to be sure that one has this bacillus unless it has been obtained from the organs of a typhoid patient. In order to say that a germ from another source is identical with the typhoid fever bacillus it is necessary to make a very careful comparative examination, not of any one property but of all the properties of the organism, and to make use of all sorts of culture media. Doubtless it will appear in the full reading of his paper that Dr. Vaughan has done this. The test with litmus milk, which Dr. Vaughan has not mentioned, is perhaps the most useful of any one single test. It is only one of many tests, but it gives valuable information. I should like to know how the germs which Dr. Vaughan has found react with litmus milk.

Dr. Vaughan's statement that a number of bacteria obtained originally from water appeared to be very unlike the typhoid bacillus—presenting, for instance, a thick, yellowish growth—and that the same bacteria, when obtained from the animal after inoculation, grew like the typhoid bacillus, is, if confirmed, an interesting and remarkable observation. There is, however, a possibility of fallacy there which he has probably had in mind. A great many of these bacilli produce intestinal changes, and under these circumstances the bacillus coli communis is very likely to enter the organism. In this case one can readily obtain from the spleen and other organs the bacillus coli communis which may be mistaken for the microörganism injected.

Dr. Vaughan is perhaps somewhat more impressed with the extent of variation of the Eberth's bacillus than I have been. It is perfectly true that one may obtain from the spleen of typhoid fever patients a number of different bacilli, and as a rule one can obtain in cases of typhoid fever, not, perhaps, so often from the spleen as from the kidney and lung, the bacillus coli communis. It is a regular invader in typhoid fever, and there is no doubt in my mind that a number of those who have written about the characters of the typhoid bacillus have been working with the bacillus coli communis and not with Eberth's bacillus.

It is interesting that Dr. Vaughan has found so large a number of the waters suspected of producing typhoid fever to contain organisms capable of killing animals when inoculated from beef-tea cultures. They were mixed cultures, I presume. Unless one adopts the view of Dr. Vaughan, which is at present hardly likely to obtain general acceptance, that typhoid fever is not due to any one specific germ but to a variety of more or less related germs, it is difficult to see what the bearing of these experiments is upon the etiology of typhoid fever. I am not prepared to go to the length of thinking that all

these germs can be changed over into germs that may produce the same results as the typhoid bacillus, and still less that they may, under certain conditions, acquire all of the morphological and cultural properties of the Eberth bacillus.

Dr. Vaughan: There is one important part of this work which I have not been able to do, and which it seems to me deserves to be done. If I could have had a number of spleens from the persons who had been drinking of each of these waters, it would have helped me very much. This is what I want to get in the next set of waters that I examine. I have been able to examine the bacteria of the spleen in only one or two instances. When this is done I think all will be able to decide positively whether typhoid is due to one specific germ, or whether there are varieties of the typhoid germ.

As to the use of the term "toxicogenic," I mean it to be indefinite. I have no right to say positively that one of these germs will cause typhoid fever, because I have not tried it on man, and the disease that we get in the lower animals is not typhoid fever. I do not want to say that these germs are capable of producing any disease, and still I want to distinguish them from germs which do not grow at 38°, and which are capable of producing poisons outside but not inside of the body. Probably it is just as well to adhere to the word "pathogenic;" but, it seems to me, that to save the word pathogenic from meaning nothing, it would be better to use the word toxicogenic.

With reference to the proof-tests with the coli commune: I have studied this germ right along with the coli commune and Eberth's bacillus all the while, and have made proof-tests. I am satisfied that none of these germs are the coli commune, and none of the germs that I have gotten from the spleen are the coli commune.

Some have said that I do not believe that one case of typhoid fever will cause another. I have never said anything of the kind. There is no question that the great epidemics in the cities generally start from the pollution of the drinking water with typhoid stools. Certainly if people drink the stools of a typhoid patient, an epidemic of typhoid fever may appear. But I do believe, and I think I have good reasons, derived from both laboratory and clinical experience, that typhoid fever may originate without a preëxisting case of typhoid fever. The conditions under which one studies this subject makes all the difference in the world. Most of you see this disease in the city. I see it principally in the country. I have seen cases of typhoid fever scattered among the farming population, among men, women, and children who have not been off their farms for weeks; and it would take a good deal to convince me that there was a common source of infection in these cases. I know that some will say that there has been a walking case of typhoid going through the country and that he has polluted all these wells, but I do not believe it. I believe there are different germs, or different varieties of the same germ, that may cause typhoid fever, and that they are widely distributed.

I am satisfied that a tolerance for these germs is very easily acquired, and

this has suggested itself to me as a possible explanation of the spread of typhoid where there are apparently no cases. If man acquires a tolerance as easily as the lower animals do, he may be drinking water containing the typhoid germs and be excreting the germs constantly from his bowels without having any typhoid fever, and thus scatter the disease. Of course, I do not know that this is true, but I know that the lower animals very readily acquire a tolerance. I also know that if I establish a tolerance for one of these germs—for Eberth's germ, for instance—I have established a tolerance for all four. This is further evidence that these germs are related in some way.

THE TREATMENT OF TYPHOID FEVER BY COLD BATHS.

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On looking over the proceedings of this Association since its commencement, I saw that as yet the cold-bath treatment of typhoid fever had not been brought prominently before it. This I considered a sufficient reason for my now bringing up the subject on the small number of cases that I have had to report on, and of eliciting the views of this Association on such an important subject.

The advantages of the application of cold water have been very ably treated of by Dr. Porcher at our first meeting, but my success in the use of cold-water baths has so convinced me of their superiority in suitable cases over all other methods, that I feel it my duty to add my testimony to that of the many others who have, with such forcible arguments in their favor, advocated this method of treatment.

I am quite well aware that many members of this Association are as ardent supporters of the use of the cold bath as I am; several, I know, have so expressed themselves at previous meetings, and have had greater experience in its application; indeed, it was owing to the very enthusiastic manner in which Dr. J. C. Wilson spoke of it to me, and the recorded history of his cases that I saw at Philadelphia, that determined me to give it a trial. I feel quite satisfied that as the result of that trial I have saved some lives, that I fear I could not have done with any other treatment. I form this opinion partly from the average mortality of the other most successful methods of treatment, as well as from the individual characteristics of some of the very bad cases that yielded to the bath treatment. The total number of cases upon which this paper is founded is thirty-nine, with

two deaths. The thirty-ninth case, which was fatal, occurred after I had commenced the preparation of this paper. Of this number seventeen were under the care of my colleague, Dr. Stewart, who has kindly permitted me to make use of them, and who, I may say, is quite as warm an advocate of the baths as I am. There are very few physicians, I think, who carry out this treatment properly, who would feel justified in relying upon any other, especially in serious cases, unless there are certain contra-indications present. Yet we see that in England, which may be justly called the birthplace of cold-bath treatment, there are very few physicians who systematically make use of it.

It is over one hundred years since Currie advocated its use there. It evidently died with him, as we have no record of its continuance. As almost every medical student knows, it is to the teachings of Liebermeister, Ziemssen, and Brand, especially the latter, that we are indebted for its re-introduction into therapeutics. Liebermeister suggested that written instructions be given to the nurse as follows: A bath to be given if the temperature is 104° or above, between 7 and 11 P.M.; 103° or above, between 12 and 3 A.M.; 102° or above, between 4 and 7 A.M. The temperature, he advises, being taken about every two hours in the night-time, sometimes even more frequently. During the daytime he seldom orders the bath unless the temperature rises above 105°. In cases in which the cold bath fails to reduce the temperature, or where contra-indications exist, he administers antipyretics.

Brand advises the bath to be given every time the rectal temperature reaches 102.4° without regard to the time of day. He advises placing the patient in water at a temperature of 68°, keeping him there for fifteen minutes, applying cold applications to the head, and using friction over the body. At Lyons this treatment of typhoid fever seems very popular, both in hospital and private practice. Bouveret, one of the hospital staff there, suggests trying the bath with the water at a higher temperature, say 80° to 85°, and if that is not successful using the colder bath of Brand. By this method of treatment and the occasional use of antipyretics, he has been able to reduce the mortality to 7.3 per cent. Dr. Hare, of Brisbane Hospital, who seems to have had a very large number of cases, by adhering strictly to Brand's rules, in one report of 1173

cases has had a mortality of 7.8 per cent. (*Practitioner*, March, 1891, p. 170.)

During the first six months in which I made use of the cold baths, I adopted Liebermeister's method. Since then I have adhered to Brand's method with slight modifications. In the first place I very seldom keep the patient in the bath longer than ten or twelve minutes, and place him there only when the temperature in the mouth reaches 102.6°. Secondly, if the patient comes under my care late in the disease, or if there are any marked symptoms of weak heart, I place him in a bath of 80° and lower the temperature with ice to 68°, and keep up friction over the body. In the cases in which I made use of the bath I proceeded as follows: With respect to hospital practice, as I very seldom have more than two or three patients at a time requiring this treatment, I have one bath-tub filled for each patient, the same water as a rule being good for twenty-four hours. The bath-tub is wheeled alongside the patient's bed and kept there. A rubber air-pillow is placed in it to support his head; ordinary bathing trunks are placed on him, and in most cases he is lifted into the tub. It has so happened that we have had patients weighing over two hundred pounds requiring this treatment. Necessity has compelled us to allow them to assist in getting into the bath; whilst in it, cold-water compresses are placed on the head or the water poured over, and at the same time another assistant applies friction to the surface of the body. Sometimes, whilst in the bath or just before it, half an ounce to one ounce of whiskey is given, either in milk or water.

The patient is kept in the bath a length of time corresponding to the fall of the temperature, as after he is in it five minutes the temperature is taken. If falling rapidly he is taken out or as soon as that is observed. In the thirty-ninth case, just referred to, the temperature fell on one occasion within the five minutes from 103° to 97.4°; of course, he was removed at once. In another case—that of a fat woman weighing over 200 pounds—the cold bath seemed to have very little effect, even a bath of twenty minutes' duration; this she had several times, the temperature falling less than one degree until after she had eight or nine baths, when it fell two or more degrees on each occasion. This woman was one of the rare cases in which the patient seemed to really enjoy the bath treatment.

Although the temperature in the early stage of the disease fell only a fraction of a degree, she always expressed herself as feeling much better.

When the patient is considered to be sufficiently long in the bath, he is lifted out and placed on a dry blanket, his trunks removed, covered up, and left for half an hour, when he is wiped dry and his temperature taken. This is almost always found to be two or three degrees below what it was previous to the bath. The exceptions to that rule are very rare. It occurred in only two cases out of the thirty-nine recorded in this paper. Of this number, twenty-one were treated by placing the patient in water at a temperature of 68° ; in the other cases the temperature of the water was 80°, reduced to 68° whilst the patient was in the bath. The immediate effect of the bath was that in one case the average reduction of temperature was 1° ; in two cases, about 2° ; in nine cases, between 2° and 3° ; in twenty-six cases, between 3° and 4° ; in one case, over 4°.

The last case was one in which the patient came under my care with a badly damaged heart and dicrotic pulse, on the sixteenth day of the fever. He had but seven baths, all of short duration. The pulse seemed to improve slightly, notwithstanding which he died of syncope on the seventh day after admission. The pulse in 95 per cent. of the occasions on which the bath was used, fell within half an hour after being removed from the bath, sometimes only two or three beats, but usually more than that, on some occasions as much as eighteen beats.

Unfortunately, I have not been able to get a reliable record of the amount of sleep in most of the cases, nor of the amount of urine secreted ; but whether the patient slept or not, the almost universal rule was that he was resting quietly where previously he was restless, and in those cases in which notes had been taken regarding sleep it was found that in most of them they had a sound and refreshing sleep, probably of short duration but always invigorating. In those cases in which the baths were stopped on account of the fever temperature not being sufficiently high to require one, according to the rules, the patients very rarely rested as well, notwithstanding that sponging with cold water was made use of. In the nurses' notes of the progress of these cases, it is a common observation,

"Patient is not resting quite as well," and it is also a point to which they have frequently drawn my attention.

Although the refreshing effects of the bath are usually present, it is very rare, indeed, to find any patients who like the treatment. They often object, sometimes vigorously. That occurred twice last summer. One case was that of a man whose temperature kept up very high, requiring numerous baths. He had seventeen in three days. On one of these days the temperature was several times over 104°, so that he had eight baths during one space of twenty-four hours. On each occasion the temperature was brought down to between 100° and 101°. After fourteen out of the seventeen baths he had a refreshing sleep, varying in time from half an hour to two hours and a half. Notwithstanding this, he commenced to object at about the fourteenth bath, and during the time that the seventeenth bath was being given him he growled and complained so bitterly and with so much noise that I was obliged to order them to be stopped, and substitute sponging. Even this he objected to. After the discontinuance, he still continued to improve. His temperature only touched normal on the nineteenth day after the last bath. During the whole of this time he was much more restless than whilst having the baths. Another patient, who was delirious, resisted the first bath so violently that it was not attempted again. Both these cases did well.

The only fatal case, besides the one I have referred to in the previous part of this paper, that I have had so far was that of a man twenty-one years of age, who was said to have been ill only four days previous to entry into the hospital, but must have been longer so. There was then found to be present double broncho-pneumonia with albuminuria. Both pulse and respiration were very rapid. Nervous symptoms rapidly made their appearance. Twenty-four hours after admission he was delirious, and twelve hours later subsultus tendinum was present. The temperature, which was 104.4°, was brought down to 103° by the bath, but rapidly rose again. The baths were repeated on seven different occasions during four days, without much apparent relief. He died on the fourth day.

I have been rather sceptical about the possibility of aborting a case of typhoid. Even yet I am not convinced that such a thing can be done, but in a family in which I had three other well-marked

cases, during my absence from town one child, at that time the second case, became ill with fever, headache, diarrhœa, etc. The father of the child, to whom I had related my success in the use of cold water in hospital practice, and as I had been contemplating its use in the first case, took upon himself the responsibility of putting into practice in his family the method I had been speaking about to him. This he did with the consent of the physician temporarily in attendance. He adhered strictly to the rules of Brand, with the result of complete subsidence of the fever in seven days. The development of two other cases in the same family, all of whom had been subjected to the same source of infection—well-water in a country place—considerably strengthened my suspicions of this so-called aborted case being one of typhoid also. The other three cases averaged about six weeks' illness each, although they all had baths; the one that had most baths, however, had two serious and prolonged relapses.

So far, the greatest number of baths which I have given any one person is thirty-five. This was in the case of a child nine years old. The entire number were given within ten days. In one period of twenty-four hours eight baths were made use of. He used to sleep tranquilly nearly the whole time between the baths, but when his temperature fell below the standard requiring them he was much more restless.

I have not yet adopted the routine of treating every case of typhoid by cold baths. During the period in which these thirty-nine cases were treated I had nine others under my care of a mild type, the temperature not being persistently high, which were treated on the expectant plan successfully. I am not yet convinced of the advisability of treating every case of typhoid with cold baths, although last summer I had one case which, for the first fourteen days, appeared to be one of the mildest type and which subsequently proved one of the most serious under my care, except that she ultimately recovered. I believe now that had I used the cold baths in her case the serious symptoms might have been averted; when they appeared, it was with the contra-indications of the bath.

The case was that of a girl nineteen years of age, whose temperature for the first fourteen days never rose above 102.2°, the lowest limit requiring the bath. There were no indications of any serious disturbance of the digestive tract.

Her general condition was remarkbly good in every respect until the appearance of an alarming hemorrhage on the fifteenth day. After this time her temperature rose considerably above the bath limit, at times reaching 104° with a weak and rapid pulse, and also several subsequent alarming hemorrhages. With this condition it was now too late to commence the bath treatment. Nervous symptoms became subsequently a prominent feature in her case. Paralysis of the pillars of the pharynx, paresis of both lower limbs, and loss of the deep reflexes were observed. Her symptoms on the eighth week resembled in many respects the pareses following diphtheria. It was only after the tenth week of the fever that these symptoms began to improve. As stated before, it is more than possible that the cold-bath treatment in this, at first, mild case might have so modified the nutrition of the ulcerated patches as to have prevented the hemorrhages.

The question naturally arises, How is the tendency to hemorrhage affected by the cold bath? Hare, to whom I have already referred, who has written a very instructive and now well-known article, states that in the large number of cases (1173) in which he made use of the cold bath, whilst the actual mortality from hemorrhage is somewhat less than those treated on the expectant plan, the occurrence of hemorrhage was "as frequent (though not more so) under the bath treatment." The experience of most of the German authorities is somewhat more favorable, as with them the occurrences of hemorrhage have been less frequent. Theoretically, it seems to me it ought to be so.

We know that fever always interferes with the process of nutrition and repair in all the organs of the body—in some it causes actual waste, whilst in others it simply modifies their functions. The capability to resist the bacillary invasion of the typhoid bacilli and the consequent sloughing of portions of the affected areas in the bowel is seriously impaired by the high temperatures. When we lower the temperature, although we do not destroy the bacilli, which in the earlier stages of the disease may be actively at work, we place the affected areas of the bowel in a much better condition to resist the effects of extensive sloughing. Where the nutritive processes are not embarrassed by the abnormal temperature its defensive struggles against the bacilli are more effectual, and the bacilli, although probably gaining ground during the first few days, do so only by a truly ulcerative process, *i. e.*, molecular necrosis, in which the *vis medicatrix naturæ* manifests itself by protecting with granulation tissue the

elements in the immediate vicinity of the ulcer. To put my meaning in fewer words: with continued high temperatures we should expect larger sloughs, with exposure of vessels; with intermittent elevations of temperature, the necrosis is molecular and the vessels stand a better chance of being protected by granulation tissue. The cold bath almost invariably reduces the temperature two to four degrees. This frequently means a normal temperature. In that case we produce an intermittent fever. True, this intermission is usually of but short duration, but the more closely we cause it to resemble that type of fever, so far as temperature is concerned, the less likely are the secondary effects of the fever, which constitute the real danger, to make their appearance. Continued high temperature, as is well known, besides causing degenerative changes in the heart and voluntary muscles, affects also the parenchyma of the glandular organs.

Nor does the central nervous system escape being profoundly affected with wide-spreading injurious effect by these high temperatures. We have ample evidence of this by the continuous headache, stupor, delirium, and what is of even greater importance than these, the blunted sensibility of the various reflex nerve-centres. In some of these conditions time is all-important. Two or three hours less of a high temperature is an immense saving to the patient. We all know that three or four hours' duration of a temperature of 104° or over has a much more serious effect than a temperature of, say, two degrees lower, lasting three or four times as long. Here we see the marked beneficial effect of the cold bath. Frequently have I seen a patient with a temperature of 104°, with a heavy, dull expression, dry and brown tongue, weak heart and rapid pulse, and with slightly increased frequency of respiration, after a bath of 68° resting quietly in sound, natural sleep, with a temperature reduced to 99° and a pulse nearly always reduced in frequency, often as much as fifteen beats, and also increased in volume. Of course, the temperature will rise again, sometimes shortly after the bath, at others after a longer duration of time, but the patient has had an interval of rest that is of inestimable value to him.

Now there is no other remedy with which I am acquainted that will produce all these improved symptoms. True, many of the antipyretics will reduce the temperature quite as much as the bath,

but none of them as rapidly and as certainly. They are all attended with some more or less objectionable features. My experience has been that almost invariably the patient sleeps for a short time after the bath. If not sleeping he is quietly resting. One of our graduates who had typhoid last January, under the care of my colleague, Dr. Stewart, and was treated by him with phenacetine and other antipyretic drugs and the cold baths at different times, is most enthusiastic in speaking of the soothing effect following the bath. Like most patients, he dreaded them on account of their immediate effect, but says there is no comparison between the after-effects of the two methods of treatment. He says that the phenacetine, whilst reducing the temperature, sometimes as much as the bath, did not give as much relief from restlessness and anxiety. He felt that the bath had a decidedly refreshing and invigorating influence.

It is a popular belief amongst the laity, in which I fear many physicians shared until very recent years, that the cold bath will tend to produce mischief in the respiratory apparatus, *i. e.*, the patient will "take cold." As most of us know now, quite the reverse is the case. Liebermeister draws particular attention to his experience in this respect. With him, in the cold-bath treatment, the percentage of cases presenting respiratory complications was much less than in any other method of treatment, and also amongst these lung troubles there was a much lower percentage of mortality. Dr. Hare's experience was still more favorable than that of Liebermeister. Fatal cases occurred in only one-fourth the number of those treated by him by the so-called expectant method, which included cold sponging and the occasional administration of antipyretics. These different results may be accounted for by the slightly different methods of treatment. Hare followed strictly the rules laid down by Brand, whereas Liebermeister adhered to the method mentioned in the early part of this paper.

In the commencement of my cold-bath treatment I followed the suggestions of Liebermeister, but since then I have adhered more closely to Brand's instructions with apparently better success. In the early part of last month a patient was brought into hospital under my care, apparently in about the eighteenth day of the disease, suffering from diarrhœa and a slight cough; his tongue very dry and brown, pulse weak and rapid, and broncho-pneumonia affecting both

lungs, and marked dulness behind in the left infra-scapular region, besides a large amount of albumin and diminished secretion of urine. I rather dreaded the bath treatment and for four days tried quinine, phenacetine, and salol, with free use of stimulants. Notwithstanding this, the temperature continued to rise, the urine to diminish in quantity, and the physical evidence of lung complication to increase. The continuation of these three symptoms, with the absence of cough corresponding to the extent of lesion, determined me to try the cold or rather cool bath. I had patient placed in water at a temperature of 80° and reduced with ice to 68°, whilst in the bath friction was used. Placing him in the water at once started vigorous coughing, with free expectoration. His temperature fell to 99°, pulse-rate to 88. This treatment was repeated every time the temperature rose to 102.4°, with the result that the amount of urine was increased in twenty-four hours from twelve ounces to twenty-four and thirty-eight the following day—more than double what it had been during the previous six days he was in the hospital. The albumin diminished in quantity. The lung symptoms at once commenced to improve. Gradually the bronchi became emptied of the mucus, and the air-vessels cleared up rapidly; the tongue commenced to lose its glazed appearance. After the sixth bath the temperature kept below 102°, and about ten days afterward he began to convalesce and is now well. In this case, during the four days patient was in hospital before the bath treatment was commenced, his temperature never went below 101.8°, nor his pulse-rate below 100, although he was sponged every four hours. A detailed statement of the few baths he had may be of interest to you and may be taken as an example of their effects in nearly all other cases.

Before bath.	Temp.	Resp.	Pulse.	Duration of bath.	30 minutes after bath.		
					Temp.	Resp.	Pulse.
April 11, 6 P.M. . .	103.4°	24	112	13 min.	99°	28	88
8 P.M. . .	105.2	32	124	12 "	101	28	94
April 12, 11 A.M. . .	102.8	32	108	12 "	98.2	28	108
2 P.M. . .	103.8	34	124	10 "	100.2	32	108
6 P.M. . .	102.8	30	110	10 "	99	26	92
8 P.M. . .	103	28	110	11 "	98 3	24	90

The following ten days' temperature kept below 102.4°, hence sponge baths only were required; temperature remained normal after the tenth day.

Whilst writing these notes (May 12th) I have a convalescing case of pneumonia treated only by cold baths. I may be excused mentioning it here, as I think it has a direct bearing on the benefits of the bath in high temperature from any cause. This young man came under my care two days after the initial rigor, and when I saw him first his temperature was over 104°. I will refer to the bath treatment only so far as the fever, respiration, and pulse-rate is concerned.

Before bath.	Temp.	Resp.	Pulse.	Duration of bath.	30 minutes after bath.		
					Temp.	Resp.	Pulse.
May 7, 2.30 P.M.	104.2°	32	100	12 min.	99°	24	84
May 8, 9.30 A.M.	104	36	116	11 "	99.4	32	88
2 P.M.	104.8	40	100	12 "	100.5	26	88
6 P.M.	104	28	120	12 "	99.8	28	78
May 9, 10.15 A.M.	104	30	100	12 "	99.8	26	90
May 10, 6 P.M.	104	32	92	13 "	98	26	78

No more baths were given after this, as the crisis occurred on the following morning, with improvement in all the physical signs.

To quite understand the rationale of these events in typhoid fever we must consider the cause of the respiratory troubles in this disease. This is not very far to seek in the weak heart, which may produce very varied conditions. That the central nervous system is affected we have ample evidence. Amongst others, the activity of the vasomotor system is impaired. The degenerating heart muscle pumps blood with enfeebled power into both systems. The impaired vasomotor activity manifests itself in the lungs in a twofold manner. It affects both the bronchial and pulmonary vessels. The blood circulates slowly in the relaxed vessels. In the bronchial arteries we have evidences of this sluggish movement of the blood in the catarrhal condition of the bronchi and bronchioles, as the result of which they may become ultimately choked up. A blunted sensibility of the nervous system, with probably weak respiratory muscles, prevents mucus being expectorated, with a resulting collapse of that portion of the lung; or the right side of the heart may be the faulty

one, with a resulting congested state of the branches of the pulmonary vessels in the alveoli of the lungs, developing probably a troublesome pneumonia. Usually both sides of the heart are involved in the respiratory troubles, producing a more or less complete bronchopneumonia. Now, as was shown in the case just related to you, and in many somewhat similar cases that have been under my charge, they are the kind of cases in which the baths, instead of being injurious, are especially suitable. The contact with the cold water invariably produces deep respirations, thus avoiding the tendency to collapse of the lung. Coughing is induced, the mucus plugs are expectorated, and the overstrained heart is relieved, and what is more the heart itself is stimulated.

These facts I consider as of great importance in showing how closely the nerve-centres are related to many of the more serious symptoms present in this fever. There can be no doubt but that high temperatures alone seriously impair the nutrition of the centres, hence the serious complication just named. That the cold bath has a local cooling effect is self-evident. That local effect is soon transmitted to the internal organs, as after the first effect of contact with the cold medium the vessels which were contracted become widely dilated and expose much more of the blood to the cooling influence of the water. The effect of the application of the cold water to the surface of the body is observed in another way. As is well known to everyone, as just stated, it causes contraction of the bloodvessels. This means temporarily increasing the blood-pressure, and thus stimulating the heart to increased work. As a consequence, the blood which has been lazily coursing through the internal organs, crowding their venous system and interfering with the functions, is forced to move on, thus relieving the tendency to congestion. This, I think there can be little doubt, accounts for the increase of the urinary secretion almost always observed in these cases, as was the case also in the one just related by me. I think we have here a very plausible explanation for the continued fall of temperature after removal from the bath. The diminished secretion of urine during the febrile state must mean retention of poisonous material in the blood, as the result of the bacillary invasion. A restoration of this secretion is probably, therefore, one of the factors in the elimination of the toxines produced by the bacilli. That typhoid fever is a com-

plex febrile state is demonstrated by the range of temperature in the earlier stages: we have the regular rise produced by the bacillary growth, followed by the irregular temperatures, the result of absorption of their products, *i. e.*, the toxines produced by the suppurative micrococci, which accumulate to a greater extent in proportion to the diminished secretion of urine.

With respect to contra-indications, the most important are those accidents which may arise in the course of the disease, and which require rest as one of the means of treatment. This applies to hemorrhage from the bowels and also to peritonitis. A very weak heart with a dicrotic pulse will require great caution. If there has been long-continued high temperature there is almost certain to be a degenerative condition of the muscular structure of the heart, and consequently the sudden determination of blood to the heart as the result of the first contact with the water may so embarrass it as to cause serious or alarming symptoms. This occurred in one case which, however, did well ultimately, the patient becoming unconscious in the bath, but on immediate removal was much improved by it. This patient had a number of baths subsequently, with no unpleasant results.

This paper really represents a mortality of two out of forty-eight cases, of which number thirty-nine had been treated by cold baths; the remaining nine were of a milder type than those treated by the baths, except the one case in which there were hemorrhages, to which I have referred at length.

I have not attempted to go into statistics, as the number of cases that I have had is not sufficiently great to be of service, nor have I attempted to give a systematic treatment of typhoid. I simply wish to add my testimony to that of many other members of this Association, who on previous occasions have incidentally, in their discussions, advocated the employment of cold baths or referred to its advantages. It is a fact which cannot be denied, that in about 90 per cent. of the occasions of pyrexia, in which it is systematically used, it will reduce the temperature, lessen the pulse-rate, and frequency of respirations, and increase the daily amount of urine secreted, besides promoting, if not actually causing, sleep.

I venture to submit that there is no other remedy in our materia medica, the use of which will as surely and quickly present all these favorable and most desirable results.

DISCUSSION.

Dr. Osler: I will give briefly our experience with this method of treatment at the Johns Hopkins Hospital. From the opening of the hospital in May, 1889, until July 1, 1890, we treated the cases symptomatically. There were thirty-two cases, with seven deaths. This was an unusually high mortality, which is accounted for in large part by the very serious nature of the cases—just such a run of serious cases as we are all accustomed to see in all forms of acute diseases. For instance, three of these cases died of perforation within a few days after admission. One case had hemorrhagic nephritis, and a fifth case had extensive croupous pneumonia.

From July 1, 1890, to February 1, 1892, there were one hundred and seven cases treated rigidly by the Brand method. The temperature of the bath was 70°, and all cases were treated indifferently except where there were certain serious complications. The patients were bathed every third hour, when the temperature rose above 102.05°. There were only eight deaths. One of these cases in which the diagnosis of typhoid fever was not made was not treated. He was an old man, aged seventy-three years, and came in in a moribund condition, with consolidation of the right lung, and it was not unnatural to make a diagnosis of pneumonia. In any case he would not have had the cold-bath treatment. The death-rate was practically that which has been obtained by the Brand method, in all of the general hospitals in which it has been employed. In the garrison hospitals the percentage is lower than this—two and three per cent.—but in the general hospitals of Europe the mortality has been reduced to seven per cent. Of these 107 cases, only 89 received the cold bath. In the others, the temperature did not rise to a point at which they were indicated.

Cold baths do not always reduce temperature, and there are cases treated under the most favorable circumstances which pursue a course almost uninfluenced by the baths. It is very interesting to note historically that Nathan Smith, in his article on *The Treatment of Typhus Fever*, written in 1823 or 1824, advocated, in a very interesting way, the treatment of the fevers by cold, and practised it as early as the summer of 1798, very shortly after its introduction by Currie.

Dr. Kinnicutt: While admitting, as we all must, that in no disease are statistics more misleading than in typhoid, which varies very much in its severity from year to year; nevertheless, a very distinct impression exists in the minds of those who have most used this method of treatment of its very great value. I am sorry that I have not the records of St. Luke's Hospital for the past few years, where this method of treatment has been adopted. In my own wards, all cases for the past few years have been treated in this way, and with exceedingly favorable results. My clinical experience corresponds very closely with that of Dr. Osler and the author of the paper.

As to its use where catarrhal conditions of the bronchi and air-cells exist, I have repeatedly had cases of catarrhal pneumonia associated with the typhoid process that have done exceptionally well under the cold-bath treatment. The greatest number of baths I have ever given in a single case is 175. This case was of such exceptional gravity and hopelessness that the question of discontinuing the baths was discussed. It was decided to continue them. The patient is at present doing full duty as a nurse in the hospital.

Dr. William Pepper: It is unnecessary to add anything to what has been stated, save for the purpose of expressing personal convictions as the result of advancing observation of this important subject. My own opinion has certainly become very definitely in favor of the treatment of high temperatures in typhoid fever by cold baths carried out strictly after the manner of Brand. It is a matter of regret that this treatment has not sooner become adopted in America. I am sure that in Pennsylvania we should long ago have paid more heed to the remarkable work accomplished by Dr. Hiram Corson, of Montgomery County. In spite of the disadvantages attending the use of cold-water bathing in country practice, and in spite of any general sympathy with the method such as now exists, this truly remarkable man, who graduated in 1828, has, for more than half a century, carried out this line of treatment in the high temperatures of infectious diseases. Some of his results have been published, and from personal knowledge I can attest many of the remarkable cures he has effected.

I feel, also, that we owe much to Professor James C. Wilson, of Philadelphia, for the forcible and convincing manner in which he recently brought before the profession the advantages of Brand's method. It is unnecessary to quote statistics merely to add to those already known.

One question which now merits discussion is, whether baths should be used in every case of typhoid fever. Opinions, of course, would differ as to the exact degree of temperature at which their use becomes obligatory. But if, as seems to be conclusively shown, there are usually no practical disadvantages connected with the use of baths if properly administered, it should be remembered that, even in cases of typhoid fever which seem mild and in which the temperature is low, there may occur sudden and wholly unexpected elevations which quickly induce bad results. The experience of all of us will confirm this, and my own feeling is drifting strongly to the view that systematic bathing should be adopted as an essential part of the treatment of all cases of typhoid fever, save in the rare instances where special contra-indications may exist. It is of the first importance that this method of treatment should become applicable in private practice. Thus far our statistics have been derived wholly from hospital sources. I am glad to say that in Philadelphia a well-known druggist, Mr. Frank E. Morgan, has agreed to keep in stock portable bath-tubs of light and strong make, which will be thoroughly convenient for use in private families. A hose will accompany the bath-tub, and also a small force-pump, by means of which siphon action

can be readily started, and the tub can thus be emptied, as required, by any convenient outlet.

I do not wish to ignore the value of other modes of applying cold water externally. We have all frequently obtained excellent results in severe cases by the thorough use of sponging, or of cold-water packs. These latter in particular, if vigorously and persistently employed, are of high efficacy. It will be found, however, that both patient and nurse generally prefer decidedly the bath to the pack, while the results obtained from baths are more reliable and effective. Whether it is the pack or the bath that is being used, systematic friction and massage of the entire body during its administration is of the first importance. I have satisfied myself that if this is omitted the best results cannot be obtained; while, on the other hand, I think there is greater danger of bad effects from shock without proper reaction.

Dr. I. E. Atkinson: There is one point in the history of typhoid fever that I think will always prevent our getting the statistics down to a desirable point of lessened mortality. There are a certain number of cases in which the temperature may never reach 102.5°, and yet are fatal. These will probably never come under the influence of the cold-bath treatment as at present conducted. I have now a case which threatens to die, in which the temperature is constantly below 102°. The members of the Society may remember some statistics published by German authors, whose names I unfortunately forget, of typhoid fever treated during the Franco-Prussian War, in which an exceedingly large number of fatalities were reported in a series of cases where the temperature did not reach 102°. These are cases which do not occur very frequently, but which do occur often enough, probably, to keep the mortality at from five to eight per cent., in spite of any antipyretic treatment that may be adopted. At the same time I wish to speak with the most unqualified approval of the cold-bath treatment, from my own experience.

Dr. W. G. Thompson: I have had forty-eight cases during the last two years treated by the Brand method, very thoroughly applied. Prior to this I was very much opposed to this method of treatment, because I well recollect as a hospital interne, many years ago, seeing cases of typhoid bathed by the older method, which consisted of putting them into a tub of water at 90°, and gradually cooling off without friction, leaving them in the tub a considerable length of time and using the thermometer as an indication when they should be taken out. The success was not good. Two years ago I undertook the Brand method, and the results are much more satisfactory, and I have reached the point where, if I had the disease myself, I should insist on being treated in this way.

I was somewhat surprised that Dr. Wilkins did not emphasize more the benefit of friction. It seems to me that the value of the Brand method of treatment from the physiological standpoint is certainly a double one, that we apply a shock of cold to a very large surface of the body, which is a strong

stimulant, and then we supplement this by a mechanical stimulant over an equally large surface. It does not seem to me that the reduction of the temperature is by any means the principal good obtained.

We can hardly attribute the results of the baths as due to the modification in the cutaneous circulation, because the object of this friction is practically to prevent the blood from being driven out of the peripheral vessels into the centre of the body. The skin is usually quite raw, and the superficial capillaries are well filled with blood. I think the danger of internal hemorrhage, by driving the blood from the periphery to the internal organs, is altogether a theoretical one. I have seen in this series of forty-eight cases three instances of hemorrhages from the bowels occur, but I could not attribute them directly to the baths; they had no immediate relation to the giving of baths. It is useless, I think, to draw conclusions from statistics of such a limited number of cases. However, there were only three deaths in forty-eight cases—a mortality corresponding to that given by Dr. Osler, or something less than 7 per cent. The previous mortality in the hospital was 19.4 per cent.

I should like to ask Dr. Wilkins, and also Dr. Osler, whether they have regarded the occurrence of menstruation, during the administration of baths, as a contra-indication for their continuance.

Dr. James Tyson: I desire to refer briefly to the cause of death in two cases of typhoid treated in this manner, as this aspect has not been touched upon by other speakers. The first case occurred in our early experience with this treatment, which is now the exclusive treatment for typhoid fever in the Hospital of the University of Pennsylvania. The man died one week, at least, after the baths had ceased to be used, the temperature during that time not reaching 102.2°. He died of embolic pneumonia. The circumstances were these: After the temperature had ceased to reach 102.2 it was thought by those in attendance—I happened to be absent for a few days—that the man was in danger of heart-failure, and hypodermic injections of strychnine were administered. Numerous abscesses followed at the sites of injections, and pneumonia shortly supervened. At the autopsy we discovered a number of embolic foci, and no other cause of death could be found.

The second fatal case was one of peritonitis, succeeding perforation. The patient was a coachman, admitted on the tenth day of the disease, and he died on the seventeenth day. He was exceedingly opposed to the treatment. We insisted upon it, and apparently the case progressed favorably until perforation suddenly occurred and he perished. This was confirmed by autopsy.

We have had no cases of hemorrhage in our experience, and, therefore, do not know the effect of this treatment upon it. It is, however, plain, from the second case, that perforation is not prevented.

I was somewhat surprised at the importance attached by the speakers to friction of the patient while in the bath. I confess I had not thought that it was of very great consequence. At first thought one would hardly suppose that any of the usual effects of friction, of which, perhaps, the attraction of blood to the surface is the chief, could be produced in a decided degree on a

patient submerged in water at a temperature of 68° to 70° F. My own idea has been that it served rather to amuse the patient. I may, however, be mistaken. It is invariably used in connection with the treatment at the University Hospital.

Dr. Stockton: It is not clear in my mind about the relation between the temperature of a patient and the employment of the bath. Of course, the rule is well understood; but it occurs to me that there are not a few cases which are benefited by the employment of baths, even though the temperature at no time reaches 102.4. It seems to me that this influence is owing to some other effect than that immediately following the lowering of temperature. If this is true, might not those severe cases, running a course without high temperature, be benefited by the bath, even though the temperature was not above 102° or 103°. I have seen cases where it seemed to me the employment of the cold bath, under these circumstances, had favorable results. I also think we find undoubted benefit in the employment of the cold bath where the temperature does not remain lowered for any length of time.

Dr. Wilkins: I believe friction is very important. There is no question that the cold pack will reduce the temperature, but it is not likely to improve the tone of the nervous system in the same way as the cold bath with the use of friction. The cold bath and friction have the efficacy of not only cooling the blood, but the further effect of imparting tone to the vessels which has been lost by high temperature. These high-temperature fevers always have a paralytic effect on the vasomotor system. The blood circulates through the capillaries in this case very much as if it were passing through rigid tubes; there is the want of the contractile element. By cooling the blood it stimulates the vasomotor centres, and in that way the alternate contraction and relaxation of the vessels of the skin is kept up; but it would not be kept up by the continuous application of cold water without friction.

With regard to menstruation, I have not had cases in which women were menstruating that required this treatment for typhoid, but I think I should feel inclined to make use of the bath in these cases. My recollection is that it is not a contra-indication.

I have had none of those cases to which Dr. Atkinson has referred—cases of continuous low temperature—but I do not see any objection to the administration of a bath in these cases, especially when combined with friction.

A BRIEF SUMMARY OF THE CLINICAL HISTORY AND TREATMENT OF TWO THOUSAND AND TWELVE CASES OF ALCOHOLISM, OF WHICH EIGHTY-SEVEN WERE MANIACAL.

By THOMAS S. LATIMER, M.D.,
OF BALTIMORE.

In the spring of 1891, at a meeting of the Johns Hopkins Hospital Medical Society, I reported 958 cases of alcoholism occurring at the Baltimore City Jail, between April 11 and December 30, 1890, of which 40 were cases of mania-à-potu, with an average duration of mania of forty-eight hours. In these cases no distinction was made between mania-à-potu and delirium tremens. They were simply cases of mania due to alcoholic excess, accompanied, in most instances, by hallucinations of abhorrent nature, with tremors, great feebleness, loss of appetite, vomiting in many cases, and inability to sleep. In the non-maniacal cases all the symptoms related were uniformly present, including tremor, except the mental disturbance. All were treated with potassium bromide; the maniacal cases with 30 grain doses every two hours, and the non-maniacal with the same drug and dose at intervals of four hours. No addition was made to this treatment, except in three or four cases, in which 10 drops of tincture of digitalis and 5 grains of carbonate of ammonia, at intervals of three hours, were also given; all recovered.

Since reporting these cases I have had opportunity to observe in the same institution 1054 additional cases, of which 47 were maniacal. This report, therefore, may be said to be a brief history of the gross clinical features and treatment of 2012 cases of alcoholism, of which 87 were maniacal. No attempt is here made to discuss the pathology of alcoholism, nor any of the symptoms, except those directly con-

nected with debauch in the habitual drinker. No reference is therefore made to symptoms presumably due to persistent hepatic, renal, or peripheral nerve lesions. Nearly all of these patients were arrested for drunkenness and disorderly conduct. They were technically called "peace cases" to imply that they were arrested for breaking the peace. A majority of them were also what in the jail are called "regulars," from the regularity with which they were returned after very brief absence.

Two noteworthy facts are contained in the above statement:

1st. They were all drunk when arrested, and many of them had not yet become sober when brought to jail.

2d. They were cases of almost continuous drunkenness, culminating at short intervals in a severe debauch, leading to some act of violence, or to a condition of drunken stupor, in which they were picked up on the streets quite helpless, and almost or quite unconscious.

It was, also, quite common for my hospital steward to say: "Doctor, this man, or woman, is a chloral fiend," or an "opium fiend," or a "cocaine fiend." Indeed, they were quite indifferent as to the particular intoxicant, using one or the other as chance might determine. All used some form of alcohol when obtainable, but many were habituated to the use of other intoxicants of the class mentioned. This fact primarily determined the choice of the remedy uniformly directed.

It will be observed that here was a particularly unfortunate class of cases to treat. Although many were young in years, all were old sots; many had had numerous attacks of mania-à-potu; many were addicted to the use of intoxicant drugs. Many were the subjects of chronic alcoholic lesions and of other loathsome and enfeebling diseases indirectly connected with their mode of life. They were, as a class, badly fed, badly clothed, and badly housed when not in jail or in the almshouse, and certainly no luxuries were furnished them at either of these places. Almost without exception, even with those who were not at any time delirious, they were without desire for food, often nauseated, sleepless, full of pain—muscular and articular—tremulous in tongue, hands, and legs, and full of nameless terror. In no single instance that I remember was the appetite for stimu-

lants lost. Almost invariably they begged piteously for drink, which in no case was given them.

The jail fare consisted of weak coffee with coarse brown bread for breakfast: some kind of soup—not very rich—with plenty of brown bread and a chunk of poor meat, which had been boiled with the soup, for dinner. No supper. They slept in locked cells, on a sack of straw on an iron bedstead, without a blanket, even in quite cool weather of spring and fall. No pneumonic or pleuritic complications ensued from this exposure.

The second series of 1054 cases, of which 47 were maniacal, presented substantially the same history, were treated in the same manner, and with the same result. Besides these, two fatal cases occurred. In one instance, the patient was brought in after my daily rounds in a condition of alcoholic coma, and died before I saw him. He was supposed by the officers of the jail to be in that heavy drunken sleep so common with these subjects, and was left to sleep off the effect of his potations without having been given anything whatever. He was found dead in his cell in the morning, apparently without having recovered consciousness. Whether this was a purely alcoholic effect, or if he had taken also, or alone, an overdose of chloral or morphine, or whether it was uræmic coma, cannot be said, as I did not see him during life, and no post-mortem examination was permitted.

The second fatal case also came in the evening, after my rounds. He was said to be quite drunk, but was able to walk to his cell, which was on the sixth tier. He became somewhat delirious in the night, but not sufficiently so to make the night officer think it worth while to change him to a cell on the ground floor, where all cases with mania are kept. In the morning, when his cell was opened, he sprang over the railing and fell to the stone pavement, receiving such injuries as to cause his death within a half-hour.

Neither of these deaths can, therefore, be fairly charged to the plan of treatment, nor are they included in the 87 cases of mania-à-potu, since, as I had not seen them before death in the first case, nor before fatal injury in the second, I am unable properly to refer them. In the second series of cases, 4 were characterized by great mental excitement, noise, and violence, without terrifying delusions. They, like all the rest, had been drinking up to the

time of arrest, and were given no alcohol after arrest. Thirteen of the second series (of 47) were admitted with delirium tremens, and in the remainder (34) delirium developed after admission; in but one case as long as seventy-two hours after admission. In no case did the delirium last more than five days. The average period at which these patients were enabled to do some kind of light work was about two days after treatment was begun; they were not then in such condition as to be declared convalescent, or, in private practice, to be allowed to leave the house; but here, where they were under constant observation, and where no opportunity to obtain drink existed, they were allowed to do such work as they desired, and all drugs were then generally stopped. On the second night usually, not until the third often, they slept fairly well; and by this time also began to eat, with apparent relish, the coarse prison fare. Food was offered them at each meal, but no attempt was made to urge it upon them if inclination did not prompt them to eat. In a very few instances, milk, eggs, light bread, and tea were substituted for the regular prison fare, but were seldom taken, and were stopped usually when appetite returned and a good sleep had been had.

No distilled or fermented drink was given in any one of these cases. No drug was administered but the bromide of potassium, except in a few instances in which great cardiac weakness prompted the use of tincture of digitalis (10 drops) and ammonium carbonate (5 grains); occasionally, in very noisy subjects, morphia ($\frac{1}{4}$ grain) and atropia ($\frac{1}{100}$ grain) were administered hypodermically at night. Thus it is seen that in 2012 cases of chronic alcoholism with acute explosions, 87 of which were maniacal, under circumstances of the most depressing character, all did well without the use of alcoholic stimulants. My conviction is strong that it was to the withholding of the alcohol, rather than to the administration of the drug, that the good results obtained were primarily due. No restraint, further than keeping them in a locked cell while delirious, was practised. They walked the cell incessantly, and often destroyed the bedding in pursuit of imaginary enemies; but as it was of but little value they were allowed to do so, rather than to bind them in bed, or even to secure the hands. As the patients were usually alone at night, in a dark cell, I found that when they were bound it added greatly to their terror, and intensified the maniacal symptoms. I am, more-

over, convinced that the unceasing walking, with its resulting weariness, tended to the induction of sleep at an earlier period than would have otherwise occurred. In no instance, beyond a few slight bruises, did any harm result from the absence of bonds. I have not observed that alcoholics are ever disposed to injure themselves. When injury is sustained, it is in flight from imaginary evils or in struggling to obtain drink. All attempts to secure the patient in bed, to bind or muffle the hands, are unnecessary. If he is securely locked in a cell or room to himself, made bare of all superfluous articles, he is unlikely to harm himself. Friends or attendants within call or sight reassure him when his hallucinations are terrifying, but he needs no restraint from them, and may be allowed to wander about his apartment without let or hindrance, with advantage to himself, provided the windows are secure.

I have treated a number of cases of delirium tremens in private practice and in hospitals during this period, but with no such results. Fatal cases are not uncommon in hospital, and quite, though less, frequent in private practice; and this, I believe, is mainly attributable to the fact that neither at home nor in a general hospital is it possible to withhold stimulants or such drugs as morphia or chloral, from consideration to other inmates of the home or ward. It must, however, be remembered that cases that are carried to hospitals have usually some diseased complication, while the merely drunken and disorderly are taken to police stations and thence to jail.

It may be well to add, before closing this short report, that nearly all of these cases were committed to jail for thirty days, and that this brief period of enforced abstinence exerted no appreciable influence on the disposition to intemperate use of strong drink, since they almost invariably returned in from one to three months, and often within as many days, after release.

The study of these cases leads me to the following conclusions:

1st. That the clinical phenomena attending excesses in the use of alcohol are the direct result of over-stimulation, and are not due to the abrupt withdrawal of the stimulus.

2d. That though ability to swallow and retain stimulants is frequently wanting, the desire for them almost uniformly persists.

3d. That alcohol in any form or quantity is unnecessary in the treatment of such cases, and is usually hurtful.

4th. That the absolute and immediate withdrawal of alcohol is of the first importance in the treatment of all the symptoms due to its excessive use, even in cases characterized by great feebleness and inability to partake of food.

5th. That forced feeding is rarely necessary, and is of doubtful utility in most cases.

6th. That for the protection of the patient no kind of bonds is called for, and, when necessary for the protection of others, or for the contents of the room, they injuriously affect the mental state of the patient.

DISCUSSION.

Dr. G. M. Garland: I would like to ask if vomiting of blood is at all frequent in alcoholism. I have had two cases in my own practice in which vomiting of large quantities of blood occurred, and in one case with fatal result. One was a middle-aged man who had been on a prolonged debauch, and during his effort to stop drinking began to vomit blood and continued to do so for some hours, when this symptom subsided and the case went on to recovery. The other was a young man about twenty-five years of age, of superb physique, who was accustomed to occasional debauches. He had been on a debauch for four or five days. He endeavored to stop on a Saturday forenoon, and at 11 o'clock that night began to vomit blood. Became very restless, constantly moving about in bed; had no especial pain; died at 10 o'clock next forenoon. The autopsy revealed no lesion in the alimentary tract. There were one or two slight spots of congestion and a slight amount of blood left in the stomach and bowels. There was nothing to explain the bloody vomiting unless there was some change in the constitution of the blood which allowed of free leakage. I have never seen anything of the sort described in connection with alcoholism.

Dr. Latimer: I have observed vomiting of blood in but one case, and that was obviously from the throat, from retching. I should infer that the vomiting of blood must frequently occur in chronic alcoholic subjects who are the subjects of sclerosis of the liver.

Dr. Osler: Such a case occurred in my practice in Philadelphia. A man who had been on a prolonged debauch had eaten heavily and taken a great deal of stimulant at his club. On his return to his house, at 1.30 A.M., he was taken with severe vomiting and hemorrhage from the stomach, from which he died before 8 o'clock in the morning. He had well-marked cirrhosis of the liver. I would like to ask if there was any evidence of liver or portal engorgement in Dr. Garland's case, and whether the œsophageal veins were engorged?

Dr. Garland: I do not know about the œsophageal veins. Nothing was found in the abdomen.

PRACTICAL RESULTS OF BACTERIOLOGICAL RESEARCHES.

By GEORGE M. STERNBERG, M.D.,
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Science does not demand practical results, but investigates for the purpose of establishing facts and explaining phenomena. And bacteriology, as a branch of natural history, is entitled to equal consideration with other departments of scientific research. Indeed, the low organisms known as bacteria offer many advantages for the study of fundamental biological problems, and the researches already made have borne abundant fruit from a scientific point of view.

But medicine is eminently practical in its aims, and practising physicians, as well as intelligent laymen, are apt to meet every announcement of a new discovery in pathology with the question: "Does it aid in the cure of disease?" Heretofore the bacteriologist has been compelled to admit that the demonstration of the specific cause in a considerable number of infectious diseases, which has been obtained through his researches, has not resulted in the discovery of a specific treatment for these diseases. At the present moment we are in possession of experimental data which open up to us a vista of possibilities in specific treatment unsuspected a year or two ago. We shall presently give a somewhat detailed account of the experimental data referred to, and will indulge in some speculations as to the practical results which are likely to follow this remarkable addition to our knowledge.

The title of my paper calls also for some reference to practical results of another kind—viz., in the prevention of disease.

Without doubt, preventive medicine, or "sanitary science," as it is sometimes called, has been immensely benefited by the researches of bacteriologists. It is true that sanitarians had obtained, by observation and by empirical methods, important data upon which to

found their recommendations before we had any knowledge of pathogenic bacteria. But it is also true that in the absence of this knowledge their recommendations were often inadequate and contradictory, and were without the authority which comes from an exact experimental basis.

In practical disinfection, for example, agents were often employed which have since been shown to have but little value, or agents of value were employed in inadequate amounts. Again, in the absence of any precise knowledge of the nature of the infectious agent or of its special habitat, the sanitarian often devoted himself to the destruction of imaginary germs in the air, and failed to attack pathogenic bacteria in the sputa of patients with pulmonary tuberculosis, in the excreta of those with typhoid fever, etc.

To-day we have an exact knowledge of the usual habitat, and of the biological characters of a considerable list of pathogenic bacteria; and this knowledge enables us to formulate recommendations which, if carried out, would doubtless go far toward eradicating the diseases induced in man, and in the lower animals, by these infecting agents. For example: the demonstration that tuberculosis is an infectious disease due to a bacterial parasite—the bacillus tuberculosis—at once leads to the recommendation that this bacillus be destroyed wherever it may be found external to the bodies of infected individuals. The fact that it is present in the sputa of patients suffering from pulmonary tuberculosis, in the milk of tuberculous cows, and in the tissues of tuberculous animals, leads to the more specific recommendations that the sputa of tuberculous patients should be disinfected, that cow's milk from an unknown source should be sterilized before it is used as food, and that the flesh of tuberculous animals should not be used as food. Finally, our knowledge of the action of numerous disinfecting agents, as tested upon this bacillus, enables us to give specific directions as to its destruction; and as we have experimental evidence showing that the tubercle bacillus is quickly destroyed by the boiling temperature, we may permit the use of milk from an unknown source after it has been boiled.

Again, we may point to the present position of aseptic surgery and midwifery. In the absence of precise knowledge relating to the microörganisms concerned in traumatic infections, Lister devised his spray apparatus for destroying pyogenic bacteria in the air during

an operation. We now know, as the result of carefully conducted experiments, that this was an unnecessary precaution, and that it would not have been efficient if the microörganisms to be destroyed had been present in the air in considerable numbers, as was imagined by the illustrious originator of antiseptic surgery. And, having learned that the great danger of infection results from the transfer of pathogenic bacteria to wound surfaces by the hands or instruments of the surgeon or his assistants, that pyogenic bacteria are found on the surface of the body and of the mucous membranes in healthy persons, and that sterilization of the hands of the surgeon, or of the surface through which his incisions are to be made, can be effected by certain procedures which have been elaborated by the experimental method, aseptic surgery takes its place as a rational method founded upon scientific observations. Thus, prevention of infection becomes the first duty of the surgeon and of the obstetrician, as well as of the physician and sanitary official. And the necessity for treating infected wounds, puerperal septicæmia, or local epidemics of infectious diseases, in the light of our present knowledge, is a reproach which attaches to some individual or corporation.

But the members of this Association are so familiar with the practical results of bacteriological studies, so far as preventive medicine is concerned, that it is unnecessary to insist upon this point. Nor need I do more than advert to the considerable success attending the use of antiseptics in traumatic infections and in localized infectious processes when these are accessible to local treatment.

Among the practical results of bacteriological researches we may mention the early diagnosis of certain infectious diseases by methods which serve to demonstrate the presence of the specific infectious agent. Thus, the presence of the tubercle bacillus in material coughed up from the lungs is now generally accepted as evidence of pulmonary tuberculosis, although this may not be revealed by the usual physical examination. In diphtheria, where the diagnosis is uncertain, a microscopical examination of the exudate, together with culture experiments made by an expert bacteriologist, may settle the question. In suspected cases of glanders in horses the diagnosis may be established by inoculating a guinea-pig with pus from a suppurating gland, as recommended by Loeffler. And in tuberculous cows an early diagnosis may be made by injecting into the suspected animal from 30 to

40 centigrammes of Koch's tuberculin. If the animal is tuberculous a decided febrile reaction occurs in from twelve to fifteen hours; and this is even more marked in early cases, in which the diagnosis by other methods is most difficult, than in advanced cases. The reliability of this test has been demonstrated by extended experiments made, for the most part, by veterinary surgeons in various parts of Europe.

Here we might stop a moment to refer to the practical results which have been obtained in France, and elsewhere, in protecting domestic animals from certain infectious diseases to which they are subject by Pasteur's method of inoculation with an attenuated virus. But it is our intention to limit the scope of this paper to human pathology. The inoculations made to prevent the development of hydrophobia in persons bitten by rabid animals, however, require brief mention; for, although the specific infectious agent in rabies has not been demonstrated, and the inoculations made do not involve the use of bacteriological methods, the discovery of their prophylactic value is a result of preceding bacteriological researches.

We give below two tables,[1] one showing the results of inoculations made at the Pasteur Institute in Paris during five years—1886 to 1890; the other a classified statement showing the results in a single year—1890:

	Number treated.	Died.	Mortality. Per cent.
1886	2671	25	0.94
1887	1770	13	0.73
1888	1622	9	0.55
1889	1830	6	0.33
1890	1540	5	0.32
Total	9433	58	0.61

In the following table, A includes all persons treated who had been bitten by an animal proved to be rabid, B persons bitten by animals examined by veterinary surgeons and pronounced rabid, C persons bitten by animals suspected of being rabid. The figures relate to the year 1890:

	Number treated.	Died.	Mortality. Per cent.
A	416	0	
B	909	4	0.44
C	215	1	0.46

[1] From the Annales of the Pasteur Institute, vol. v. pp. 345 and 346.

But, as announced at the outset, the principal object of the present paper is to bring to your attention certain recent researches which lead to the hope that we are on the eve of a new departure in the specific treatment of infectious diseases.

As is well known to the members of this Association, the researches of bacteriologists have established the fact that the pathogenic action of those bacteria which have been shown to be concerned in the etiology of specific infectious diseases is due to the formation of toxic products during the active development of the bacterial cells. The discovery of these toxines and toxalbumins has led to a line of research work, the object of which is to isolate and study each of these toxic products separately by the methods of chemistry and of experimental pathology.

In the course of these experiments, and of the extended researches which have been made with reference to the explanation of natural and acquired immunity, the remarkable discoveries which will occupy our special attention have been made.

The discovery of the "antitoxines" is so recent, and the facts relating to their specific antidotal power so unexpected, that I may be permitted to go into some detail with reference to the experimental data which form the basis of our present knowledge.

The demonstration by Nuttall, Buchner, and others, that the blood-serum of certain animals possesses decided germicidal power, led to researches with reference to the nature of the particular substance to which this action is due. Buchner[1] showed that it does not depend upon the cellular elements of the blood, and inferred from his experiments that it must be an albuminoid body. The researches of Martin and Hankin[2] confirmed this view. These investigators succeeded in obtaining from the spleen and lymph glands of rats—which animals have a natural immunity against anthrax—a globulin which they believe to be the active germicidal agent in the blood and tissues of these animals. Additional facts of importance were developed by the experiments of Ogata and Jasuhara,[3] who showed that the blood of an immune animal—dog or frog—injected into a susceptible animal—mouse—shortly before or after inoculating it with a virulent

[1] Archiv. f. Hygiene, Bd. x., 1890.
[2] British Med. Journal, May 31, 1890.
[3] Centralbl. f. Bakteriol., Bd. ix., 1891, p. 25.

culture of the anthrax bacillus, protects the animal from a fatal attack of anthrax, and that after its recovery from the mild attack which results the animal is immune against the action of virulent cultures. The protective influence is exercised when the blood is injected as long as seventy-two hours before the inoculation, or five hours after, and it is not lost when the blood used for the antidotal injection has been preserved for weeks in a cool place. It is completely destroyed, however, by exposing this blood for an hour to a temperature of 45° C. A single drop of frog's blood sufficed to preserve a mouse from the fatal effects of an anthrax inoculation.

It is evident that these facts, if well established, have immense significance from a therapeutic point of view; but they are so novel, and so unexpected, that we might regard the results reported with some scepticism were it not that they are supported by similar facts obtained in other infectious maladies by independent investigators. First in date and importance are those of Behring and Kitasato,[1] published soon after the results of the above-named Japanese investigators had been made public in a communication to the Medical Faculty of the Imperial University of Japan, at Tokio.

The experiments of Behring and Kitasato showed that the blood of animals which have an artificial immunity against tetanus, or against diphtheria, when injected into susceptible animals, preserves them from fatal infection with virulent cultures of the bacillus of tetanus or of diphtheria. So small a quantity as 0.2 c.c. of blood from an immune rabbit, injected into the cavity of the abdomen of a mouse, was sufficient to protect it from the fatal effects of a virulent culture of the tetanus bacillus injected twenty-four hours later. Further, these bacteriologists have shown that the toxic substance—toxalbumin—present in a filtered culture of the tetanus bacillus is neutralized by admixture with the blood of an immune rabbit. A culture ten days old was sterilized by filtration; this filtrate was found to kill a mouse with certainty in less than two days when injected into the animal in an extremely minute quantity (0.0001 c.c.). Five c.c. of blood serum from an immune rabbit was added to 1 c.c. of this virulent filtrate. At the end of twenty-four hours four mice received each 0.2 c.c. of this mixture, containing more than 300 times

[1] Deutsch. med. Wochenschr., 1890, No. 49.

the fatal dose of the filtered culture. All of these mice survived, and proved subsequently to be immune for virulent cultures of the tetanus bacillus; while four control mice, each of which was inoculated with 0.001 c.c. of the same filtrate, unmixed with blood, perished within thirty-six hours. The blood of rabbits not immune against tetanus was without result in neutralizing the toxalbumin in filtered tetanus cultures, as was also the blood of children, of calves, sheep, and horses.

Similar results have been obtained by the Italian investigators Tizzoni and Cattani,[1] who have given special attention to the study of the chemical characters of the "tetanus antitoxine," which they have isolated from the blood of immune animals. They arrive at the conclusion that it is a globulin, or a substance carried down by the globulin precipitate, and that it is different from the globulin obtained by Hankin from animals immune against anthrax.

Recently a most important experiment, from the point of view presented in this paper, has been made at Padua with the tetanus antitoxine of Tizzoni and Cattani. This was the successful treatment of a case of traumatic tetanus with tetanus antitoxine prepared by the authors named. The case is reported by Dr. Rudolf Schwarz,[2] Assistant to the Surgical Clinic at Padua.

The patient was a peasant boy, aged fifteen years, who wounded himself in the left forearm while attempting to cut a walnut which he had picked up from the ground. There was considerable hemorrhage, which was controlled by the application of a wad of spider's web and a bandage. A return of the hemorrhage induced the parents to take the boy to the Surgical Clinic at Padua. There, under appropriate treatment, the hemorrhage was arrested and the wound healed. Two weeks after receiving the wound symptoms of tetanus were developed. The patient was admitted to hospital three days later, at which time the jaws were immovable and the muscles of the arm in a state of tetanic rigidity, while other muscles of the trunk and extremities were also involved. Treatment with chloral and warm baths was without effect in arresting the progress of the malady, and on the 16th of September, nine days after admission, the patient had eight or nine tetanic convulsions during the night, accompanied by difficult respiration and slight opisthotonus. No improvement having occurred under the treatment employed, it was decided to test the value of tetanus antitoxine, which had been sent for the purpose by Prof. Tizzoni, who had obtained it from the blood serum of a dog which had been rendered "strongly immune" against tetanus. On the after-

[1] Centralbl. f. Bakteriol., Bd. ix., 1891, p. 685.

[2] Ibid., Bd. x., 1891, p. 785.

noon of September 18th, 15 centigrammes of this antitoxine dissolved in water was injected beneath the skin. The same quantity was injected the following day. On the morning of the 20th the patient was decidedly better; on the afternoon of this day he received 25 centigrammes of the antitoxine, and the same amount on the following day. After each injection there was a notable fall in the temperature. The patient continued to improve, and on the 23d all symptoms of tetanus had disappeared.

In a postscript to his communication Dr. Schwarz states that he has private information of two other patients who have recovered from tetanus under the same treatment—one in the hospital at Colle di Val d'Elsa (Tuscany), treated by Dr. Pacini; the other in the Surgical Clinic at Innsbruch, treated by Prof. Nicoladoni.

Another case has since been reported by Finotti.[1]

If further experience establishes the value of this treatment, no physician will fail to recognize the fact that medical science has taken a new departure, and that bacteriological studies have led up to practical results of the greatest importance. Nor is it likely that the therapeutic possibilities in this direction will be limited to the disease in which the successful *experimentum crucis* has been made upon man. The experiments of Behring give us reason to hope that the potent toxalbumin of the diphtheria bacillus may be neutralized in the bodies of infected individuals. Having succeeded in rendering animals immune against the pathogenic action of the diphtheria bacillus, Behring ascertained that the blood of these animals neutralizes the toxic potency of filtered cultures of this bacillus, either before or after injecting them into susceptible animals.

Another disease in which extremely promising experimental results have been obtained is croupous pneumonia. The experiments of G. and F. Klemperer[2] show that the blood serum of animals which have an artificial immunity against cultures of micrococcus pneumoniæ crouposæ—so-called "diplococcus pneumoniæ"—when injected into other susceptible animals, renders them immune; and, also, when injected into the circulation of animals inoculated with a virulent culture of this micrococcus it has a curative action, apparently depending upon its power to neutralize the toxic products to which the pathogenic effect of these cultures is due, as in the cases heretofore mentioned. The authors named found no difficulty in

[1] Wien. klin. Wochenschr., 1892, No. 1.

[2] Berlin. klin. Wochenschr., 1891, Nos. 34 and 35.

establishing immunity in rabbits by injecting filtered cultures into their tissues; but they found that this immunity was only established after an interval of several days, indicating that a certain time is required for the reaction on the part of the tissues which results in the formation of an antitoxine. But the blood of an immune animal, containing this antitoxine, when injected into the circulation of a susceptible animal, confers immunity upon it at once.

Similar results have been obtained by Emmerich and Fawitzky,[1] whose researches relate both to pneumonia and to the disease of swine known in Germany as *rothlauf* (hog-erysipelas). They report their success in arresting the fatal malady resulting from the injection into rabbits of cultures of the micrococcus of pneumonia or the bacillus of rothlauf, by injecting into these animals, after infection, the blood or tissue juices of immune animals. When the injection is made shortly before inoculation with a virulent culture, infection does not occur. As a result of their investigations the authors referred to express the hope that croupous pneumonia in man may be arrested by a similar mode of treatment.

From analogy, based upon the experimental evidence heretofore referred to, the successful treatment of tuberculosis would appear to call for the administration of an antituberculin rather than upon that of the active toxic principle elaborated by the tubercle bacillus; and already we have experimental evidence indicating that this is the case.

The Italian investigators Tizzoni and Centanni[2] have recently published a preliminary communication in which they give the results of experiments which appear to show that in guinea-pigs treated with tuberculin, by Koch's method, a substance is developed which neutralizes the tubercle virus either *in vitro* or in the body of an animal inoculated with a pure culture of the bacillus.

The facts already stated would lead to the inference that animals which have an artificial immunity against rabies, as a result of inoculation with an attenuated virus, owe this immunity to the presence of an antitoxine in their blood or tissue juices. This inference is supported by recent experimental evidence. Prof. Tizzoni and his

[1] Centralbl. f. Bakteriol., Bd. x., 1891, p. 714.
[2] Ibid., Bd. xi., 1892, p. 82.

associate, Dr. Schwarz, have published an important paper in the *Annales de Micrographie* (January, 1892), in which the following results are reported:

Blood serum taken from a rabbit which has an artificial immunity against rabies has the power of neutralizing, *in vitro*, the virulence of the spinal marrow of a rabid animal after a contact of five hours. The blood serum of dogs which have an acquired immunity against the virus of rabies has a similar action, but in a much slighter degree.

The substance present in the blood serum of an immune rabbit, to which its antitoxic action is due, does not dialyse. It is precipitated by alcohol, and preserves its activity, to a considerable extent, after being precipitated. It has the characters of a globulin. It is soluble in glycerin.

Blood serum from an immune rabbit has the power of neutralizing the virus of rabies, not only *in vitro*, but also in the body of an inoculated animal; and the experimenters named succeeded, as a rule, in conferring immunity upon susceptible animals by inoculating them with blood serum containing this antitoxine. They also obtained evidence of its curative power when injected into inoculated animals some time after the inoculation. The antitoxine of rabies, as also that of tetanus, is found only in the serum of the blood, and not in the tissues (nervous or muscular), or in the parenchyma of the various organs (liver, spleen, kidneys).

Finally, our authors state their belief that the use of this antitoxine may probably be substituted for Pasteur's inoculations with an attenuated virus, with a view to preventing the development of rabies in man after the bite of a rabid animal; and, also, that it may prove to be curative after the symptoms of rabies are developed.

I have now to refer to other investigations of great importance in their bearing upon the subject under consideration. Prof. Ehrlich,[1] of Berlin, has recently published his researches with reference to the pathogenic action of certain toxalbumins not produced by bacteria, but which are similar in composition and in toxic action to some of those extracted from cultures of pathogenic bacteria. He has shown that susceptible animals may be made immune against the toxic

[1] Deutsch. med. Wochenschr., 1891, No. 44.

action of these proteids, and that the blood and tissue juices of the immune animal contain an antitoxine to which this immunity is due.

Dr. Sewall showed[1] several years ago (1887) that immunity from the toxic action of rattlesnake venom may be produced by the previous injection of small doses of the "hemialbumose," to which it owes its potency.

In this connection we may remark that there is some evidence to show that persons who are repeatedly stung by certain poisonous insects—mosquitoes, bees—acquire a greater or less degree of immunity from the distressing local effects of their stings.

The experiments of Ehrlich were made with toxalbumins of vegetable origin, one—*ricin*—from the castor oil bean, the other—*abrin*—from the jequirity bean. The toxic potency of ricin is somewhat greater than that of abrin, and it is estimated by Ehrlich that one gramme of this substance would suffice to kill one and a half millions of guinea-pigs. When injected beneath the skin in dilute solution it produces intense local inflammation, resulting in necrosis. Mice are less susceptible than guinea-pigs, and are more easily made immune. This is most readily effected by giving them small and gradually increasing doses with their food. As a result of this treatment the animal resists subcutaneous injections of 200 to 400 times the fatal dose for animals not having this artificial immunity. The fatal dose of abrin is about double that of ricin. When injected into mice in the proportion of 1 c.c. to 20 grammes of body weight, a solution of 1 part in 100,000 of water proved to be a fatal dose. The local effects are also less pronounced when solutions of abrin are used; they consist principally of an extensive induration of the tissues around the point of injection, and a subsequent falling off of the hair over this indurated area. When introduced into the conjunctival sac, however, abrin produces a local inflammation in smaller amounts than ricin, a solution of 1 : 800 being sufficient to cause a decided, but temporary, conjunctivitis. Solutions of 1 : 50 or 1 : 100 of either of these toxalbumins, introduced into the eye of a mouse, give rise to a panophthalmitis which commonly results in the destruction of the eye. But in mice which have been rendered immune by feeding them for

[1] Journal of Physiology, vol. viii., 1887, p. 203.

several weeks with food containing one of these toxalbumins, no reaction follows the introduction into the eye of the strongest possible solution, or of a paste made by adding abrin to a little 10 per cent. salt solution. Ehrlich gives the following explanation of the remarkable degree of immunity established in his experiments by the method mentioned :

"All of these phenomena depend, as may easily be shown, upon the fact that the blood contains a body—antiabrin—which completely neutralizes the action of the abrin, probably by destroying this body."

In a more recent paper, Ehrlich[1] has given an account of subsequent experiments which show that the young of mice which have an an acquired immunity for these vegetable toxalbumins may acquire immunity from the ingestion of the mother's milk; and, also, that immunity against tetanus may be acquired in a very brief time by young mice through their mother's milk. In his tetanus experiments Ehrlich used blood serum from an immune horse to give immunity to the mother mouse, when her young were already seventeen days old. Of this blood serum, 2 c.c. were injected at a time on two successive days. The day after the first injection one of the sucklings received a tetanus inoculation, by means of a splinter of wood to which spores were attached. The animal remained in good health, while a much larger control mouse inoculated in the same way died of tetanus at the end of twenty-six hours. Other sucklings inoculated at the end of forty-eight and of seventy-two hours after the mother had received the injection of blood serum likewise remained in good health, while other control mice died.

In a recent communication (1892), Brieger, Kitasato, and Wassermann[2] have published the results of their interesting experiments with a bouillon made from the thymus gland of the calf. It was found that the tetanus bacillus cultivated in this bouillon did not form spores and had comparatively little virulence. Mice or rabbits inoculated with it in small doses (0.001 to 0.2 c.c. for a mouse) proved to be subsequently immune. And the blood serum of an immune rabbit injected into the peritoneal cavity of a mouse (0.1 to

[1] Zeitschr. f. Hygiene, Bd. xii., 1892, p. 183.
[2] Ibid., p. 137.

0.5 c.c.) was found to give it immunity from the pathogenic action of a virulent culture of the tetanus bacillus. Similar results were obtained with several other pathogenic bacteria cultivated in the thymus bouillon—spirillum of cholera, bacillus of diphtheria, typhoid bacillus.

A most interesting question, growing out of these extraordinary experimental results, at once presents itself: Does the animal which is immune for one of these toxalbumins also exhibit immunity as regards the toxic action of the other? This question Ehrlich has answered. His experiments show that animals which are immune against one of these substances are quite as susceptible to the toxic action of the other as if they did not possess this immunity—*i. e.*, the antitoxin of ricin does not destroy abrin, and *vice versa*. As an illustration of the fact, he states that in one experiment a rabbit was made immune for ricin to such an extent that the introduction into its eye of this substance in powder produced no inflammatory reaction; but the subsequent introduction of a solution of abrin, of 1 : 10,000, caused a violent inflammation.

Evidently these facts are of the same order as those relating to immunity from infectious diseases, and, taken in connection with the experimental data previously referred to, give strong support to the view that the morbid phenomena in all diseases of this class are due to the specific toxic action of substances resembling the toxalbumins already discovered, and that acquired immunity from any one of these diseases results from the formation of an antitoxine in the body of the immune animal.

In the case of a number of infectious diseases it is demonstrated that the toxalbumin is produced by a specific microörganism; but we have no satisfactory evidence that this is the case in the strictly contagious eruptive fevers. So far as these diseases are concerned, the doctrine of a *contagium vivum* rests solely upon analogy and upon the assumption that the evident increase in the quantity of infectious material which occurs in the body of an infected individual is proof of self-multiplication, which is a property of living matter only.

While fully recognizing the force of this reasoning, we must insist that the experimental evidence at present available does not justify a generalization to the effect that all infectious diseases are

due to specific microörganisms. And it seems worth while to at least stop to inquire as to the possibility of a different explanation in those diseases, such as smallpox and scarlet fever, in which there is no evidence of an increase of the specific poison outside of the bodies of infected animals, and in which a living infectious agent has not been demonstrated. Is it possible that in these diseases the toxalbumin which gives them their specific character is a product of the living cells of the body of the infected animal? Other questions which remain to be settled relate to the production and retention of antitoxines in the bodies of immune animals. Is production continuous during immunity, or does it occur only during the modified attack which results from inoculation with an attenuated virus, or of filtered cultures, the antitoxine being subsequently retained in the circulating blood? The latter supposition does not at first view appear very plausible; but it must be remembered that *these albuminous bodies do not dialyse—i. e.*, they do not pass through animal membranes—and consequently would not readily escape from the bloodvessels, notwithstanding the fact that they are held in solution in the circulating fluid.

On the other hand, the passage of the tetanus antitoxine into the mother's milk, as shown by Ehrlich's experiments upon mice, indicates a continuous supply, otherwise the immunity of the mother would soon be lost.

Evidently the production of an antitoxine during an attack of any one of the infectious diseases would account for recovery in non-fatal cases; and it may be that this is the true explanation of self-limitation in diseases of this class. If Nature adopts this method of cure, we but follow her if we seek to introduce more of the antitoxine for the purpose of arresting the progress of cases of unusual severity and fatal tendency.

In the experiments of G. and F. Klemperer it was noted that when the serum of an immune animal was injected into the circulation of an animal suffering from septicæmia, resulting from infection with mic. pneumoniæ crouposæ, the temperature was promptly reduced to the extent of two or three degrees Centigrade; and in the case of tetanus reported by Schwartz the temperature fell a degree or more after each injection.

Although the production of these antitoxines in considerable

amounts for therapeutic use will be attended with difficulties, there can be no doubt that methods will be devised for obtaining them on a large scale as soon as it is definitely established that they may be successfully used as specifics in the treatment of infectious diseases.

In diseases which are common to man and the lower animals the source from which they may be obtained is evident; but in diseases peculiar to man we do not at present see just how they are to be obtained. Reasoning from the analogy afforded by the experimental evidence heretofore referred to, we infer that the blood and tissue juices of an individual who has recently suffered an attack of smallpox or scarlet fever contains an antitoxine which would neutralize the active poison of the disease in the circulation of another person immediately after infection. Whether a small quantity of blood drawn from the veins of the protected individual would suffice to arrest the progress of the diseases mentioned, or to modify their course, can only be decided by experiment; but the experiment seems to me to be a legitimate one. Possibly transfusion of a moderate amount of blood from one to the other might prove to be curative, or, if made in advance of infection, might confer immunity. Or it may be that an antitoxine can be obtained from the blood of vaccinated calves which would have a curative action in smallpox.

This possibility I have undertaken to determine by the experimental method, and now make the following preliminary communication relating to results already obtained.

The following experiments have been made with the kind assistance of Dr William E. Griffiths, who has for many years been engaged in the production of vaccine virus in the city of Brooklyn, and consequently is an expert in the vaccination of calves and in recognizing vaccinia in these animals:

Upon visiting Dr. Griffiths and making known to him my desires, I found him quite willing to assist me, and also that he had a recently vaccinated, and consequently immune, calf in his stable. This animal had been vaccinated in numerous places upon the abdomen and thighs fourteen days previously. The vaccination was entirely successful, and a large number of quills had been charged from the vesicles which formed. At the time of my visit for the purpose of collecting blood serum from this animal, dry crusts still remained attached at the points where vaccination had been practised two weeks previously. On the 28th of April I collected blood serum from a

superficial vein in the hind leg of this calf. This blood was placed in an ice-chest for twenty-four hours, at the end of which time the clear serum was drawn off in "Sternberg's bulbs." Four drops of this serum were placed in each of two small, sterilized, glass tubes; in one of these we placed three quills charged with fresh vaccine lymph from a calf. At the end of an hour the quills were removed, after carefully washing off in the serum the lymph with which they had been charged. In the other tube we mixed with the four drops of blood serum an emulsion made from a fragment of a perfectly fresh vaccine crust from the arm of a child; this was crushed upon a piece of glass and rubbed up with a little of the same blood serum. The two tubes were now placed in an ice-chest for twenty-four hours, at the end of which time the contents were used to vaccinate a calf purchased for the purpose. Dr. Griffiths carefully shaved the thighs of this calf and scarified each thigh in several places, as he is accustomed to do in vaccinating for the propagation of lymph. The contents of the tube containing lymph from the quills was rubbed into the scarified places upon one thigh, and the contents of the tube containing the emulsified crust into the other. On the 8th of May, nine days after the vaccination, the calf was carefully examined, and it was ascertained that the result of the vaccination was entirely negative.

Evidently it was necessary to make a control experiment before we would be justified in ascribing this negative result to a neutralization of the virus by some special substance present in the blood serum of an immune calf. Possibly the blood of a non-immune calf might also, after an exposure of twenty-four hours, neutralize the specific virulence of vaccine lymph. The control experiment was made as follows:

On the 9th of May we collected blood from a vein in the leg of a non-immune (not vaccinated) calf; this was placed in the ice-chest for twenty-four hours, and the following day clear serum was collected in Sternberg's bulbs. Three quills charged with fresh lymph from a calf, of the same lot as those used in the previous experiment, were placed in four drops of this blood serum in each of two small glass tubes. As in the previous experiment, the lymph was washed from the quills at the end of an hour, and the tubes were placed aside in the ice-chest. At the end of twenty-four hours the serum in these two tubes was used to vaccinate the same calf which had served for the previous experiment. Several points were scarified upon the left thigh and upon the left side of the abdomen, which were carefully shaved for the purpose.

At the same time the animal was vaccinated upon the right thigh and upon the right side of the abdomen with virus mixed with blood serum from the immune calf. This serum, collected in Sternberg's bulbs on the 28th of April, had since been kept in the ice-chest. One hour before the vaccination four drops of this blood serum were mixed with one drop of liquid lymph,

which had been recently collected by Dr. Griffiths in a capillary tube from a vaccinated calf. At the same time, three quills charged with bovine lymph were immersed in four drops of the same blood serum—from immune calf. As stated, the animal was vaccinated upon the right side of the abdomen and upon the right thigh with this virus, which had been exposed for one hour to the action of blood serum from an immune calf. The serum containing the liquid lymph was rubbed into the scarification on the right side of the abdomen, the serum containing lymph from the quills into the right thigh. On the 19th of May, eight days after the vaccination, the animal was carefully examined by Dr. Griffiths and myself, and the following results noted: Upon the left thigh and left side of the abdomen the vaccinations—from quills in non-immune blood serum after twenty-four hours contact—were entirely successful, the scarifications being surrounded by characteristic vesicles and covered by characteristic crusts. Upon the right thigh—vaccinations from quills immersed in blood serum from immune calf for one hour—and upon the right side of abdomen—vaccinatious with liquid lymph mixed with blood serum from immune calf—the result was entirely negative. Several of the scarifications had entirely healed; others were covered with a dry scab which was easily detached, and under which the scarification was healing without any appearance of vesicles such as surrounded the scarifications upon the left side.

The result of the experiments made is, therefore, very definite, and shows that the blood serum of an immune calf contains something which neutralizes the specific virulence of vaccine virus, either bovine or from humanized lymph—crust from the arm of a child.

It is my intention to follow up this line of investigation, to endeavor to isolate this antitoxine of vaccinia, and to test the question of its possible specific action in neutralizing the smallpox virus in infected individuals, either before or after the development of the disease.

DISCUSSION.

Dr. W. H. Welch: There can be no doubt as to the scientific fact that the blood-serum of immunized animals may possess powerful therapeutic effects. As regards the practical application of this principle to the treatment of human beings, it does not seem to me that we as yet possess positive results entirely free from doubt as to the correctness of the interpretation put upon them. The most striking results which have thus far been reported regarding the application of this new method to human beings come from the Italian observers in the treatment of tetanus, and there are various reasons why these results should not as yet be unreservedly accepted as proof

of the efficacy of this mode of treatment in human beings. There is, however, every reason to persevere in experimental work in the direction indicated. The experimental results of Dr. Sternberg regarding the antitoxic power of the blood-serum of vaccinated calves are most interesting, and we may look forward, doubtless, to further communications from him on the subject.

Dr. Kinnicutt: It is difficult to judge in regard to the accuracy of the reported results of the Italian cases. The last case, the sixth one, is the most convincing. It was a well-developed case of tetanus. The urine, on the evening before the injection of the antitoxine of tetanus, was injected into a series of five or six guinea-pigs and rats. In all, it is claimed, death followed in twenty-four hours, with well-marked symptoms of tetanus. On the third day after the daily injection of from twenty-five to fifty centigrammes of the antitoxine, the urine, when injected into a series of animals, was found to be innocuous. The blood, also, was injected, before and after the treatment with the tetanus antitoxine, and with similar results. It seems to me that this is the fullest, and perhaps the most convincing, of the reports which have been published. Some anti-tetanus toxine is being prepared in the Pathological Laboratory of the College of Physicians and Surgeons of New York, and, whenever the opportunity offers, its effects will be very critically studied.

Dr. Vaughan: I wish to express my high appreciation of Dr. Sternberg's paper, and especially of his own experimental work with regard to vaccine. Of course, the number of experiments is too limited, as yet, for positive conclusions to be drawn. We are now all convinced of the fact that it is comparatively easy to give animals immunity against a certain germ for a very short time. It can be done with the attenuated germ, with the chemical products of the germ, and it may be done with other substances which are not produced by the germ. Of course, it will take time to solve all these problems, and we must be very slow to conclude that all of this is going to be of special benefit in medicine.

Dr. Sewell is, I believe, the only one who has paid especial attention to the time over which this immunity has extended. In his experiments with the rattlesnake poison he found that he could make his birds immune, but that this immunity lasted only a few months.

It has always been a question with me whether this is not simply establishing a tolerance for a poison, instead of a true vaccine action. I am inclined to think that the action both of the toxines and antitoxines is of the nature of the ferments. No toxalbumin has ever been obtained in a pure state; we know nothing about its chemical structure. For instance, take the so-called toxalbumin of diphtheria. Inject a small quantity into animals, and a certain per cent. of them will die within a period of time that will vary with the amount injected. The only rational explanation that appears to my mind is that the substance acts as a ferment. It is not necessary for the substance to be a poison *per se*. It may, by its fermentative action, destroy certain things in the body which are necessary for the maintenance of certain cells, although

not itself poisonous. The whole subject is interesting and suggestive, and we must wait for practical application.

One other point. We all know that surgical operations have an effect upon diseases where the operation is not in itself curative. A few years ago there was a great craze about circumcision as a curative in epilepsy. I had a friend who performed the operation a great number of times. In his first case the child, who had been having epileptic seizures two or three times a day, after the operation had them only once in ten to twenty days. In course of time, however, the seizures became as bad as ever. The operation has been abandoned.

There are many ways in which immunity can be secured, and we must distinguish between producing immunity and curing the disease. There is no evidence that the two are the same, although the Klemperers try to make it appear so in their work. I think the action of Koch's tuberculin should make us a little slow about accepting and drawing positive conclusions from experimental work. Experimental immunity and experimental cure is one thing, and cure in man is another thing.

Dr. Lyman: The results of laboratory experiments have been rather discouraging as showing the transient character of much of the immunity obtained by the inoculations alluded to. It appears to me that we are not so very near, as some enthusiasts think, to the time when we shall be able to protect our patients from diseases. Vaccination against smallpox seems to be almost the only case where permanence of immunity is secured. What Dr. Vaughan has said about ferments agrees with the conclusions I arrived at twenty years ago. I think that the majority of these toxines and antitoxines are of the ferment character.

Dr. Sternberg: We know something about living ferments, but when you call these substances ferments you have not explained much.

I did not purpose to say to this Association that it had been absolutely demonstrated that tetanus could be cured by antitoxine. I merely reported the cases. I admire conservatism and scepticism, but why Dr. Kitasato should be so very conservative about the results obtained upon man when they correspond so entirely with the results which he and others have obtained on the lower animals I do not understand. When I see carefully reported cases, like that of Schwartz, in which all the symptoms are carefully detailed and the results of treatment seem to be so very definite, I feel like giving considerable credit to it without admitting that the thing is proved. I am very free to say that I think the future of scientific medicine is in this direction, and that we have entered upon a field that is to be cultivated vigorously, and which will give you results that will knock the conservatism from under your feet before many years.

I believe that there is something in the blood of the immune calf that neutralizes the vaccine virus. This rests upon very few experiments, but these are so satisfactory and decided that I am thoroughly convinced that I shall get similar results on repeating them.

THE TREATMENT OF EXPERIMENTAL TUBERCULOSIS BY KOCH'S TUBERCULIN, HUNTER'S MODIFICATIONS, AND OTHER PRODUCTS OF THE TUBERCLE BACILLUS.

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ALTHOUGH several attempts at preventive inoculation against tuberculosis had already been made by experimenters, the possibility of curing the existing disease by injections of products derived from the tubercle bacillus itself originated with Dr Robert Koch, and the gigantic human experiment which followed and resulted in so much inevitable disappointment is still fresh in the public as well as the professional mind.

The hopes to which tuberculin gave rise were entirely founded on Koch's observations of the curative influence said to be exercised by this substance over experimental tuberculosis in the guinea-pig. In the general haste to determine its efficacy in the human subject the study of its effects upon tubercular animals has received as yet but little attention; and Koch himself has never given but the most meagre details of his observations relating to this most important question.

It is quite evident, however, that if products derived from the tubercle bacillus have no beneficial influence upon the artificially-produced disease in animals, there is little reason for continuing laboratory experiments of a tentative nature on the human subject, and research must take a new direction. While, on the other hand, if these bacterial products can be demonstrated to control, to any appreciable extent, the development of experimental tuberculosis, a reasonable hope may be entertained that, by perfected methods and a more exact and extended knowledge of the various complex sub-

stances produced by germ life, the ravages of the disease in the human subject may yet be brought under control.

Moreover, the work of Hunter and the claims of Klebs would also indicate the possibility of obtaining a product free from the dangers of tuberculin, yet capable, if not of curing the disease, at least of exercising a marked beneficial influence over its course, and some evidence as to the remedial efficacy as well as the dangers of these various products as noted in animals, would tend to place our knowledge on a firmer basis, to strengthen our convictions, and to guide us to a more intelligent application of these substances to the treatment of tuberculosis in man.

The present research has been undertaken, therefore, with a view to obtaining some more definite evidence—first, as to the curative effect said to be exercised by Koch's tuberculin over inoculated guinea-pigs; second, as to the curative value and dangers in experimental tuberculosis of the modifications of tuberculin proposed by Hunter.

Furthermore, leaving to the distinguished chemists who have undertaken it, the study and separation of the various elements, remedial and injurious, contained in Koch's tuberculin, the writer has attempted by an application of the eliminative process to demonstrate, by a few simple experiments, in which part of liquid cultures of the tubercle bacillus the remedial elements reside—whether in the bacterio-protein of which the bacilli are composed, or in the albumoses and soluble toxines produced in artificial culture media as the result of their life history.

Treatment with Koch's Tuberculin.

The description of experiments will be made as brief as compatible with accuracy. Twelve guinea-pigs are inoculated under the skin of the abdomen with a pure culture of tubercle bacilli grown on glycerin serum. Four are kept as controls, and the rest are treated within two weeks of the virulent inoculation by injections of Koch's crude tuberculin, beginning at one milligramme daily and steadily increasing to one cubic centimetre, the intervals being lengthened as the doses become larger. Great care is found necessary in order not to kill the animals during treatment by an overdose of the remedy; two of them dying within six hours of taking the same

dose which they had previously borne without accident; all the animals died tubercular—the controls with an average life of 88 days, the rest of the animals of 112 days.

So far as prolongation of life is concerned, these results would indeed seem meagre, and differ but little from those obtained by other experimenters. Dujardin-Beaumetz,[1] Gibier,[2] Jaccoud,[3] Metschnikoff,[4] Roux, Bardach,[5] and Pfuhl[6] all failed to cure inoculated guinea-pigs, although Pfuhl obtained a marked prolongation of life in his test animals.

But the influence of the treatment is nevertheless strikingly illustrated by the autopsies. If a healthy guinea-pig be inoculated under the skin of the abdomen, the tissues and organs become involved almost invariably in the following order, and the disease spreads with great regularity from the inoculation point to the inguinal glands, thence to the retro-peritoneal glands, the spleen, the liver, and the lungs. Thus, in the dead controls the pathological processes are seen to be more advanced the nearer they occur to the inoculation wound, while in the treated animals the reverse usually holds true.

The controls at autopsies showed cheesy inoculation wounds often still open, cheesy inguinal and retro-peritoneal glands, enormous spleen riddled with tubercles and cheesy areas, enlarged tubercular liver, and a moderate number of young tubercles scattered through the lungs. In the test animals, if treated for more than two months, on the other hand, the inoculation spot is healed and covered with hair; the inguinal glands are firm, only slightly enlarged, and rarely cheesy; the spleen is either moderately tubercular, or may even be of normal size and appearance; the liver as well; while the lungs are solid with cheesy tubercle.

It is probable, therefore, that the curative influence of tuberculin is exercised only when tubercle tissue has once formed. And the reparative processes which it incites seem to follow in the track of the disease, but are powerless to anticipate its spread to neighboring

[1] Dujardin-Beaumetz: Sem. Med., Feb. 11, 1891.
[2] Gibier: New York Med. Journal, March 14, 1891.
[3] Jaccoud: Sem. Med., Feb. 11, 1891.
[4] Metschnikoff and Roux: Annales Inst. Pasteur, Nov. 25, 1891.
[5] Bardach: London Congress of Hygiene, August, 1891.
[6] Pfuhl: Zeitschrift für Hygiene und Infect. Krankheiten, vol. vii., No. 2, 1891.

structures. Habituation to the injection soon takes place. The dose grows rapidly as the disease overcome at one point spreads to another, and by the time the lungs are attacked anything short of a poisonous amount will no longer bring about the local reaction necessary to cure.

The pulmonary disease, therefore, progresses unchecked, and soon results in the animal's death. A fact observed in the experiments to follow strongly confirms this view. If tubercle bacilli are injected into the anterior chamber of a rabbit's eye, and the treatment by injections of a product of the tubercle bacillus be begun at once, the appearance of tubercles on the iris and cornea cannot be averted, and will be rather hastened than delayed, even though the efforts of the experimenter to effect a cure be ultimately crowned with success.

That tuberculin cannot give immunity against subsequent infection has been shown by others, and by the writer in a research published at the time of Koch's announcement of its action as a specific. It would seem, therefore, that injections of tuberculin exercise a marked remedial influence on the tubercular lesions of the guinea-pig, and can cure the primary ones. But contrary to Koch's belief, they cannot "protect the tissues from further invasion of the germs." For infection in these animals may spread from one point to another, even while a cure of the primary lesions is being effected by the treatment.

If this view be correct, the rapidity with which the disease becomes generalized in guinea-pigs would make their restoration a most trying test of the efficacy of the remedy. And it is to be hoped that Koch will, before long, give the exact details of the methods of treatment which have, in his hands, led to the cure of these most susceptible animals.

Treatment by Hunter's Modifications.

Whether the injurious elements of tuberculin can be eliminated or not, without impairing its remedial virtues, is a question at present of vital interest, and upon which the highest authorities differ. Koch[1] measures the efficacy of his product by its power to kill in certain doses tubercular guinea-pigs, and from the first has insisted

[1] Koch: Deutsche med. Wochenschr., Jan. 15, 1891.

that the curative substances are inseparable from those that produce fever and local reaction.

In his latest research, in which he was assisted by Brieger, a significant silence on this point is maintained. Klebs,[1] on the other hand, asserts that he has produced from tuberculin a material entirely free from fever-producing or dangerous effects, capable of destroying the tubercle bacillus in the living bodies of men and animals, and of curing the disease. As yet, however, he has furnished no evidence which can be subjected by others to scientific tests.

Hunter,[2] in a recent communication on the chemical constituents of tuberculin, gives the results which he has attained in producing a modified form of this substance, in terms so clear and concise as to invite other investigators to test his conclusions, and attempt to throw some additional light on the points he has so admirably studied. Guided by the effects observed in lupus he has sought, while retaining the curative substance, to eliminate from Koch's tuberculin those elements which produce violent reaction and fever, which he considers principally responsible for most of the accidents caused by this mode of treatment. As a result of his research he proposes two modifications which he designates merely as B and C B, both of which bring about in lupus certain reparative changes tending to cure, but unaccompanied by fever, and each varying greatly in the degree and intensity of the local reaction it produces.

Some light to guide us in the application of these important deductions to the treatment of human beings, has been sought by a short study of the effect of Hunter's modifications on experimental tuberculosis. In these products, has the curative element been retained? Have the substances which produce fever and uncontrollable inflammatory reactions or hasten a rapid generalization of the disease, been eliminated? Which of the two modifications is the most efficient and safe? To these questions a partial answer has been sought by the experimental method.

Experiments.

By following Hunter's clear and concise directions no difficulty was experienced in the manufacture of the two modifications he pro-

[1] Klebs: Ibid., Nov. 5, 1891.

[2] Hunter: British Med. Journal, March 14, 1891.

poses, which were obtained at first from Koch's tuberculin, and later from tuberculin made in my own laboratory. Since dialysis is depended upon in these modifications to eliminate most of the fever-producing elements, special attention was given to that part of the process. The thinest membranes possible were selected, and the full time recommended was allowed. Nevertheless, the substances obtained, especially B, were found, although producing much less fever than their equivalent of tuberculin, to invariably cause a very appreciable rise of temperature in tubercular animals; but no death occurred as the direct result of the treatment.

The details of the experiments were the same as those already described in which Koch's tuberculin was used. The results show an average life of 92 days for the controls; with one animal still living seven months after inoculation; of 89 days for the animals treated with C B; and 120 days for the animals treated with B, of which two are still living, seven months after the virulent inoculation. The living control, however, is tubercular; the inoculation wound is healed, but several large cheesy glands can be felt in the groin; he illustrates admirably the extreme limit to which the element of natural individual resistance may prolong life in inoculation tuberculosis, and the fallacy of drawing hasty conclusions as to the influence of any treatment if based on observations made upon the prolongation of life of single animals.

Two of the animals treated with C B died unusually early, namely, 63 and 78 days after inoculation. The autopsies showed a marked tendency to early generalization of the disease; emaciation was extreme; no very advanced or extensive caseous processes anywhere, but an enormous amount of young tubercle equally distributed in all the organs.

The duration of life in the animals dying while under treatment with B was considerably above the average of the controls. The autopsies showed practically the same appearance, and the same attempt at repair in the inoculation wound, glands, and spleen, as in animals dying while under tuberculin treatment.

The two guinea-pigs, which are still alive (nearly seven months after the virulent inoculation), show a healed inoculation wound, no enlarged glands, and their weight is a trifle more than at the beginning of the experiment. The dose of modification B has risen

with them to 7 c.c. at an injection; the immediate result of which is to throw them instantly into tetanic spasms, from which, however, they recover within an hour. They no longer show any rise of temperature following the injections.

From the evidence obtained by this experiment the following conclusions seem justified: 1. In Hunter's modifications the curative principle of tuberculin has been retained. This is especially true of modification B. 2. The fever-producing elements have been, to a certain extent, eliminated, but C B may favor rather than hinder the tendency to generalization. 3. Modification B is as efficient and safer than either C B or crude tuberculin. Thus far my clinical experience with modification B has confirmed this conclusion.

Treatment by Filtered Culture Medium and Bacterio-protein.

Tuberculin is a most complex mixture of many hitherto unknown organic compounds, and all attempts at solving the mystery of its chemical composition have been, as yet, only partially successful. Koch first speaks of his specific as being a 50 per cent. glycerin extract of the tubercle bacillus; while in a later communication he describes it as being obtained by the evaporation of liquid cultures. But whether the virtues of this evaporated material are due to the extraction by heat of the bacilli, or reside in the soluble products with which they have impregnated the animal broth during their growth, does not appear. What is evident is, that the whole is boiled together, evaporated by heat, the dead bacilli removed by filtration, the result being the complex mixture known as tuberculin.

To the bacteriologist, liquid cultures resolve themselves at once into two very distinct and easily separable parts, namely, the tubercle bacilli which float on the surface and the beef-broth in which they have grown. The tubercle bacilli are principally composed of bacterio-protein, which is but very sparingly soluble in any reagent, while the liquid of ripe cultures holds in perfect solution the albuminous compounds and toxines which have been formed in it as the result of the growth and development of the microbes.

It has occurred to the writer that the eliminative method might here be applied with advantage, and that the future work of the

chemist would be greatly simplified if it could be proved whether the remedial principle is to be sought in the bacilli themselves, or in the culture medium in which they have grown. And with this end in view the following experiments were carried out.

Liquid cultures of the tubercle bacillus are filtered through hardened filter paper. To this filtrate, one per cent. of carbolic acid is added to preserve it, and it is now ready for use. This fluid contains all the soluble albumoses and toxines, but no bacterio-protein, and nothing which may have been extracted from the bacilli by heat, as in the manipulation for producing Koch's tuberculin. It contains a hitherto undescribed substance which is at once precipitated by a temperature of 100° C., and which is probably of the nature of a true toxalbumin, as it is thrown down by heat and causes fever in tubercular animals. This substance is not a component part of tuberculin, as in the manufacture of Koch's lymph it must at once be precipitated by heat during the evaporation on the water-bath, and filtered off with the bacilli. Want of space forbids anything beyond a mere reference to this as yet unstudied element of filtered cultures. An extraction of the bacterio-protein may be effected according to the first plan about to be described, a partial solution according to the second.

The mass of bacilli is first thoroughly washed while still on the filter paper with tepid water. This is a tedious process, and should be carried on until the wash water no longer shows any cloudiness when added to a nitrate of silver solution (the cloudiness being due to precipitation of silver chloride, due to the chloride of sodium present in the culture medium).

The bacilli may then be transferred to a flask containing a 50 per cent. glycerin and water mixture, equal in volume to the original liquid culture made use of. The flask is put into the sterilizer for two hours, and after having been thus extracted the bacilli are removed by filtration through filter paper. This filtrate is a true glycerin extract of the tubercle bacillus, though neither in its outward appearance, nor in the effect produced by it in tubercular animals, has it apparently much in common with Koch's tuberculin.

A partial solution of the bacilli may be effected by transferring the well-washed culture mass to an excess of boiling absolute alcohol for ten minutes, filtering while the alcohol is hot, adding an amount

of pure glycerin equal to a quarter the original volume of liquid culture used, and entirely evaporating the alcohol in the dry oven at a temperature of 55° C. This glycerin solution holds a large amount of bacterio-protein, but is so viscid that it cannot well be injected without first being heated, and even then a large needle is necessary.

With these two solutions several sets of tubercular guinea-pigs were treated; the general observations made being that bacterio-protein solutions cause a slow form of suppuration at the site of injection; no marked fever, even in large doses (two to three cubic centimetres), an overdose never resulting in death even when the animals are profoundly tubercular. They produce no inflammatory reaction in and around tubercular areas, and they have, apparently, but slight remedial value. They cause emaciation and general cachexia in the animals treated.

From the autopsies the 50 per cent. glycerin solution appears to hinder the natural chimiotactic reaction at the inoculation spot or in the injected organ and thus may favor a general spread of the disease.

Injections of the soluble products contained in the culture medium in which bacilli have developed, produce no local suppuration but all the characteristic reactions of tuberculin; distinct local and general reactions of a transitory nature, death invariably following an overdose; marked improvement in the primary lesions followed occasionally by general improvement and prolongation of life, and finally death by the spread of the disease to some distant organ. By injection of this material chimiotaxis around diseased areas is greatly stimulated, a rush of serum and leucocytes to the infected part invariably resulting from the treatment.

To obtain more conclusive evidence, recourse was had to another method of experimentation. Rabbits were inoculated in the anterior chamber of the eye according to the plan first proposed by Cohnheim and Salamonsen, and adopted by Baumgarten[1] for the study of tuberculosis. In each experiment one lot was kept as controls, while the remaining animals were divided into equal lots and treated with each of the solutions. Thus, the progress of the disease in the controls, as compared with its evolution in the eyes of the treated animals,

[1] Baumgarten: Zeitschrift für klin. Med., Berlin, 1885, vol. ix., pp. 141–151.

could conveniently be watched and compared. This plan proved most satisfactory, and the evidence it brought forth is full of interest.

The Effect of Bacterio-protein Solution.

Injections of the second solution of bacterio-protein were begun from 5 to 20 days after virulent inoculation. They were followed by but slight, if any, fever, and caused no immediate and transitory irritation of the affected eye, which, nevertheless, slowly grew worse. They proved highly chimiotactic locally, producing suppuration at the site of puncture, and their prolonged use was followed by profound constitutional deterioration. The animals became anæmic, emaciated steadily, and if the treatment was pushed for a long time, often died of general cachexia.

On autopsy, the kidneys were occasionally found to present the appearance of chronic parenchymatous nephritis, and abscesses and chronic purulent pleurisy were observed. These observations confirm those of Strauss and Gameleia,[1] and Muffici,[2] who found chronic poisoning to result from injections of dead bacilli. The beneficial effect on the eye lesions was doubtful, and consisted in some cases of an apparent retardation, during the second month of treatment, of the destructive processes connected with caseation. The eyes were, however, never restored.

Effects of Soluble Products Contained in Filtered Culture Medium.

Injections of the filtered culture medium in which tubercle bacilli had been grown, produced no local suppuration; only a transitory loss of weight occurring after each injection, and no deterioration in the animal's general health resulted. They were followed by distinct rise of temperature, varying according to the dose injected and the amount of disease present, occurring within four hours and lasting from twelve to eighteen hours afterward, accompanied with marked but temporary irritation of the inoculated eye. Intense redness, iritis, purulent conjunctivitis, developed at once, and later increased;

[1] Strauss and Gameleia: Arch. de Med. expér. et d'Anat. path., Nov., 1891.

[2] Muffici: Sem. Med., Nov. 11, 1891.

tension, cloudiness of the cornea, pannus, etc., slowly supervened; the vascular phenomena distinctly remitting during the intervals between the injections, which soon lost their irritating effect on the eye unless the dose was steadily increased.

During the first six weeks the treatment appears to have only sensibly hastened the progress of the disease, but about the seventh week (if the injections were begun within a few days after inoculation) an improvement in the eye lesions first shows itself. The inoculation wound in the cornea bulges less, and is less cheesy in appearance; the cornea is less cloudy, while no new tubercular areas are seen to have formed on the iris. If the injections were begun when the eye was already extensively involved, shrinking of the eyeball and diminution of the diseased areas in the cornea are observed at this time, when destructive processes are rapidly progressing in the untreated animal's eyes.

From this time, as the irritation caused by each injection disappears, marked improvement is apparent. The caseous areas slowly melt away; the dilated bloodvessels shrink and disappear; intraocular pressure diminishes; the cornea clears, and from 12 to 18 weeks from the beginning of treatment the eye is to all appearances *cured*, in the sense that it has been restored as nearly to its normal condition as was consistent with the existing lesions when treatment was begun. The eyeball may be but a shrunken fibrous mass, or the anterior chamber alone may be obliterated; the iris normal in appearance, adhering to the now transparent cornea, or the eye may be so little damaged that its function as a visual organ is almost completely restored. As to the permanency of this apparent cure, time alone can decide. The writer has, as yet, no evidence to offer on this point, and it is not impossible that relapses may occur. But the complete restoration, even if it should prove occasionally to be but temporary, of such delicate tissues as the result of any general specific treatment, is a fact of the utmost significance and of the highest importance.

These results correspond in most particulars to those recently published by Prof. Donitz[1] and Sattler,[2] in the treatment of eye tuberculosis with Koch's tuberculin, his being the only observation as yet

[1] Donitz: Deutsche Med. Woch., Nov. 19, 1891. [2] Ibid., Nos. 1 and 2, 1892.

recorded in which any success has been attained in experimental tuberculosis by this method of treatment.

In the few autopsies made on animals whose eyes had been cured, no tubercular disease was found in the other organs. It should be borne in mind, however, that the anatomical conditions found in the eye are not at all favorable to a great spread of the local disease, or to its rapid generalization. A study of the changes taking place during the restoration of the eye points distinctly to local reaction as an inseparable element of cure. If the dose be not increased and, in consequence, the usual transient irritation be not produced, improvement ceases, and in time the tubercular disease again progresses. Attempts at eliminating from tuberculin those substances which produce local reaction would seem therefore to be of doubtful utility. It is, therefore, not to the bodies of the bacilli, but to the liquid which they have impregnated with the products of their life history, that we must look for the remedial substance contained in ripe cultures. What is extracted from the bacilli themselves by heat in glycerinated media (as in the method hitherto adopted to produce tuberculin) cannot cure, and it is not impossible that it may hasten the spread of the disease by paralyzing the normal chimiotactic reaction of the system; besides, this substance is harmful to the health of living animals. For these reasons it should not be retained. On the other hand, the soluble products contained in the animal broth in which bacilli have developed, but from which they have been removed by filtration without heat, can cure localized tuberculosis in the rabbit's eye; and it is to this element of liquid cultures that we must turn in future attempts to separate a substance free from the dangers of tuberculin and yet capable of exercising, it may be, to a greater or less degree, a curative influence over visceral tuberculosis in man.

The conclusions to be drawn from this study may be briefly stated as follows:

1. Koch's tuberculin does not cure experimental tuberculosis in the guinea-pig, although its specific influence on the primary lesions is indisputable.

2. Hunter's modification C B contains less of the remedial principle than tuberculin, and is apparently quite as dangerous.

3. Hunter's modification B is as efficacious as tuberculin, and free from some of its dangers.

4. Solutions of bacterio-protein obtained as described from well-washed tubercle bacilli have, when extracted with 50 per cent. glycerin and water, an injurious effect; when treated with hot alcohol a doubtful and, at best, feeble remedial influence over experimental tuberculosis.

5. They produce suppuration and serious constitutional impairment, which may result in organic disease and death.

6. The liquid culture medium, in which tubercle bacilli have developed, but from which they have been removed by filtration, contains the elements which bring about reaction and cure in tubercular tissue.

7. Experimental tuberculosis in the rabbit's eye can be cured by injections of the filtered culture medium.

8. The permanency of such a cure has not yet been established.

[The paper was followed by a demonstration of the curative influence of the treatment by means of photographs and living animals.]

DISCUSSION.

Dr. Kinnicutt: This is one of the most valuable contributions that has yet been made to the subject of Koch's discovery. Dr. Trudeau has certainly made a new departure. The last time when he was in New York it was agreed that he experimentally and I clinically should undertake investigations with the modifications of tuberculin that had been proposed by Dr. Hunter. The preparations were made for both of us in the laboratory of the College of Physicians and Surgeons, and they consisted of the preparations B and C B. Since that time, purposely, no communication has passed between Dr. Trudeau and myself in regard to the results of our work. We preferred to test individually the correctness or incorrectness of Hunter's observations and then compare our results, and this is the first communication that I have received in regard to Dr. Trudeau's investigations. As they are entirely experimental, it may be interesting to hear what results I have obtained clinically from the use of the same modifications.

The first proposition which Dr. Trudeau inserts in his conclusion is, that Koch's tuberculin does not cure experimental tuberculosis in guinea-pigs, although its specific influence on the primary lesion is indisputable. My clinical experience of eighteen months has convinced me that tuberculin

does contain a remedial principle; that tuberculin is a complex substance, and the remedial principle is associated with other substances which are harmful in their nature.

His second proposition is that Hunter's modification C B contains less of the remedial principle than tuberculin, and is apparently quite as dangerous. That same conclusion has been reached by me from clinical study. It not only seems to contain less of the remedial principle, but it is a dangerous modification to use. In a single case in my wards in which it was used, after an injection of eight milligrammes, an acute apex catarrh was developed almost immediately, which, however, ran a favorable course and terminated at the end of the tenth day.

The third proposition of Dr. Trudeau is that Hunter's modification B is as efficacious as tuberculin and free from some of its bad effects. That, too, has been my clinical experience. Dr. Hunter claims that this modification B is as nearly as possible a pure albumose, that it is free from the alkaloidal substances which he believes to be the harmful properties in the crude tuberculin. The clinical results that have been obtained are as follows: Seven cases of well-marked pulmonary tuberculosis were very critically observed before and throughout their treatment. In two of the cases there has been no appreciable difference in the physical signs of disease during the two or three months that they have been under treatment; although there has been an appreciable difference in the physical condition, which is improved somewhat. In one case the improvement is most marked. In the fourth case the improvement is distinct but less marked. In the fifth and sixth cases the improvement (and by improvement I mean an improvement in physical signs of disease) has been marked; and in the seventh case there has positively been an arrest of the disease. The patient, after having presented signs of infiltration at the apex of one lung, anteriorly and posteriorly, with abundant subcrepitation and other signs, is to-day absolutely free from them, and with the exception of impaired resonance he goes out of the hospital as a case of arrested tuberculous disease of the lung.

While the number of cases is much too small to enable us to express a positive opinion as to any specific action on tuberculous lesions which this modification may possess, it is large enough to indicate in the strongest manner the desirability of further investigation of its apparently specifically beneficial effects.

In regard to the liquid culture medium: of that Dr. Trudeau alone can speak. It is quite a new departure, and certainly the reports that he gives to us are most noteworthy, and it seems to me that in his work, more than in that of anyone else in this country, we are to look forward to what I believe is certainly to come—that is, a specific remedial treatment of tuberculosis.

It may be interesting to the members of the Association to know that Dr. Trudeau has made some experimental investigations in regard to the alleged specific effect of creasote in tuberculosis. His experiments have not been published, but he has very kindly given them to me to publish in connection with some work of my own in this direction. The summary of his experi-

mental work was, that creasote given in the largest possible doses in rabbits, had absolutely no effect either in the development of experimental tuberculosis or in arresting its progress.

Dr. W. H. Welch: Dr. Trudeau, if here, would doubtless express his gratification with the similarity between Dr. Kinnicutt's results and his own, so far as they relate to the same subject.

It seems to me most gratifying that the stage of newspaper notoriety in this matter has given place to quiet laboratory work, from which, as Dr. Trudeau's communication indicates, there is good reason to expect results of scientific and practical importance.

An important conclusion reached by Dr. Trudeau is that the bacterio-proteins in tubercle bacilli do not possess curative powers in any marked degree. This conclusion is in opposition to the views of Hueppe, Buchner, and others.

Dr. Trudeau, in making use of the simple filtrate of liquid tubercle cultures, uses a material not hitherto employed; hence we cannot criticise these experiments by any previous knowledge on the subject. He is properly cautious in the deduction of his conclusions. He is certainly to be congratulated upon the important and promising results which he has already brought to light and which should encourage him to continue this line of work.

MID-SYSTOLIC AND LATE-SYSTOLIC MITRAL MURMURS.

By J. P. CROZER GRIFFITH, M.D.,

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By mid-systolic and late-systolic murmurs are here designated those which possess the area of diffusion of the ordinary murmur of mitral insufficiency, and which are attended by the ordinary symptoms of the disease, but which occupy only the middle or latter portion of the period between the apex beat of the heart and the second sound, leaving the first portion unaffected.

The details of three cases which have come under my observation will, perhaps, best describe the nature of this condition.

Case I.—Emma G., aged twenty years. Married. Mill-operative. Her mother had suffered from rheumatism, and she herself had had measles, diphtheria, and typhoid fever when a small child. In 1879 she experienced her

Fig. 1.

Emma G., Feb., 1888. Mid-systolic murmur.

first attack of rheumatism, and as soon as she recovered from it began to suffer from palpitation, dyspnœa, and swelling of the feet. Her general health, however, was good, and she was able to work. In February, 1888, she came to the Hospital of the University of Pennsylvania, where I first saw her. At this time she was suffering from pain over the heart, swelling of the feet, dyspnœa on exertion, and palpitation. Physical examination revealed a loud, high-pitched, and very musical murmur in the region of the apex. The first sound was distinctly heard; then, after a slight interval, came the murmur referred to, and then, after a pause about as long as the first, the second sound. Both first and second sounds were entirely free from murmur. Exact records

of the area of diffusion of the murmur and the character of the sounds elsewhere were not made at this time, but it was carefully observed that the character of the murmur was entirely that of mitral insufficiency, though its time was purely *mid-systolic* (Fig. 1), and that there was no evidence of disease of any other valve than the mitral.

On May 28, 1888, the following note was made: "Under the use of digitalis, cod-liver oil, and iron she has improved greatly, and her heart has given her less trouble than for a long time before. At present the pulse is rather short and hard. No murmur can be heard. Both pulmonary and aortic second sounds are accentuated."

During the spring of 1888 she passed through a second attack of inflammatory rheumatism, though not of great severity.

Through the summer of 1888 her health was excellent. About the first of November, 1888, she exhibited the early symptoms of typhoid fever, and entered the Hospital of the University on the 11th of the month, coming under my care. The record at this date reads: "She has been suffering from palpitation. After rest in bed for some hours, and while still recumbent, examination shows the apex beat to be in the fourth interspace. The cardiac dulness is bounded by the third rib, the left border of the sternum, and the nipple line. Possibly a slight systolic murmur can be heard over the præcardium. The sounds are normal at the aortic cartilage, at the apex and in the axilla, but the second sound is slightly accentuated over the pulmonary cartilage, the sternum, and the xyphoid cartilage." The disease ran a favorable course, though complicated by a slight phlebitis. While still in bed, on December 3d, there was noted "a faint systolic murmur at the apex, transmitted horizontally outward for about 2 inches, not heard elsewhere. The aortic second sound ringing; the pulmonary second sound accentuated. Apex beat in the fourth interspace."

On December 18th, the following record was made: "A high-pitched musical murmur, rather closely following the apex beat but not replacing the first sound, is heard at the apex and very faintly in the axilla; but its maximum intensity is just to the left of the xyphoid cartilage. The pulmonary second sound is accentuated."

On December 27th is recorded: "An almost imperceptible systolic murmur, frequently not heard at all. Occasionally the murmur is musical, and seems to be influenced by respiration. The patient is still in bed."

Shortly after this time the patient was out of bed and about the ward, and the following note was made on January 17, 1889: "A peculiar, short, high-pitched, creaking systolic murmur is audible over the whole cardiac region, but loudest near the apex. It comes somewhat after the apex beat, and both the first and second sounds can be distinctly heard."

The patient soon left the hospital, and was not seen again until October 10, 1889. She had been suffering from no cardiac symptoms until shortly before. She now complained of debility, some uterine disturbance, palpitation, and swelling of the hands. The same mid-systolic murmur was audible as on some previous occasions.

She was seen several times up to December 21, 1889, but in spite of treatment her symptoms were not materially altered, and "the same musical murmur" is recorded.

She was not examined again until September 23, 1890. At this time she was in about the fourth month of pregnancy. She complained of swelling of the feet, headache, and leucorrhœa. The record made at this date is as follows: "At the second right costal cartilage both sounds are clear. At the second left cartilage the second sound is decidedly accentuated. Down the sternum both sounds are loud and clear. At the apex is a low-pitched murmur coming just after the apex beat. It has not the distinctive character of the

Fig. 2.

Emma G., Sept. 23, 1890. Rhythm nearly that of ordinary mitral regurgitation.

mid-systolic murmur as heard at the first examination of the patient, though it still begins slightly later than an ordinary mitral regurgitant murmur (Fig. 2) The murmur is faintly musical and is audible in the axilla and to about midway between the apex and the xyphoid cartilage. It is not heard in the back or in the vessels of the neck. The cardiac dulness extends from the third rib to just to the left of the mid-sternal line and to a little outside of the nipple line. The apex beat is in the fourth interspace slightly beyond the nipple. The horizontal diameter of the cardiac dulness equals $4\frac{1}{2}$ inches." A sphygmographic tracing of the radial pulse was taken on this date (Fig. 3).

Fig. 3.

Emma G. Pulse-tracing Sept 23, 1890.

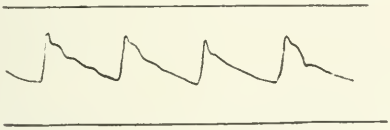
The patient was examined for the last time toward the close of February, 1891, being now very near the full term of pregnancy. A slightly musical murmur, distinctly after the first sound, was heard loudest at the apex and transmitted into the axilla. It was faintly audible everywhere over the heart. It approached the character of that heard in February, 1888, but was not separated from the apex beat by quite so long an interval.

Case II.—The following interesting case of late-systolic mitral murmur was first observed in the medical dispensary of the University of Pennsylvania by Dr. J. H. Fussell, through whose kindness I am enabled to report it. Considerable discussion at first arose among those who examined the patient,

regarding the nature of the lesion and of the murmur. Eventually all agreed that he certainly presented a mitral regurgitant murmur of a very peculiar type. I finally made a careful study of the heart sounds and recorded the following notes:

"March 17, 1890. John McG., aged seventy-two, married. He has at times had to work rather hard and to do some heavy lifting. With the exception of occasional slight dyspnœa, he appears to have been well until the age of twenty-five years. At that time he was confined to bed for three or four weeks with shortness of breath. As he recovered and got about again he found that his feet and legs often became swollen. He gives no distinct history of any attack of rheumatism, but says that he has at times had pain in his arms and oppression across the chest; the result he supposed, of his heavy work. He appears to have recovered completely from the severe illness mentioned and to have been in good health for years. About five or six years ago, however, he began to notice that in walking up a long and steep hill on his return from his day's work he would experience a dull pain over the chest, with shortness of breath and palpitation of the heart. These symptoms

Fig. 4.



John McG. Pulse-tracing March 17, 1890.

troubled him to such an extent that he would be obliged to rest several times on the way up the hill. As soon as he reached the level ground the sensations left him. At the same period he observed swelling of the feet. All his symptoms gradually grew worse, and at the present time he has swelling of the feet nearly constantly, and often has palpitation even when at rest. He suffers from dyspnœa on exercise, but is able to sleep prone. He has a slight cough and considerable headache. He has had no dyspnœa for some time and has never had hæmorrhoids. Two years ago he was operated upon for hydrocele.

"Examination shows him to be without anæmia, emaciation, arcus senilis, or pulsation or murmur in the vessels of the neck. There are no abnormal physical signs to be noted in the lungs. The urine is normal. The artery at the wrist is not notably atheromatous and shows neither increase of tension nor the trip-hammer pulse. The sphygmographic tracing confirms the evidence given to the fingers (Fig. 4). The apex beat can be felt very indistinctly in the fifth interspace within the nipple line. No præcordial thrill can be perceived. The cardiac dulness extends from the fourth rib to the right edge of the sternum, and thence transversely to the left to a little beyond the nipple line. At the apex there is a clear first sound. The latter portion, rather less than one-half, of the systolic period is occupied by a high pitched murmur,

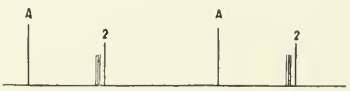
which continues almost to the second sound, ending so immediately before it, that it at first seems almost actually to run into it (Fig. 5). The second sound is, however, clear and unaffected by the murmur. The murmur is heard very distinctly in the axilla, and the second sound is a little accentuated there. Over the base the same murmur is audible, though not so loud. At the aortic cartilage no murmur can be heard and the second sound is slightly ringing. The second sound is quite loud down the sternum, and no murmur can be heard there. At the xyphoid cartilage the murmur is very faintly audible, while at the pulmonary cartilage there is neither murmur nor accentuation of the second sound."

FIG. 5.

John McG., March 17, 1890. Late-systolic murmur.

The patient was examined repeatedly after this date before the ward class at the University Hospital. At every examination the same characteristic murmur could be heard. On some occasions, however, it was so short and so close to the second sound (Fig. 6), that it was difficult to determine whether or not it was synchronous with it. Nevertheless, careful auscultation, with simultaneous timing of the apex beat or of the vessels of the neck, invariably showed that it both began and ceased before the second sound occurred. In no instance could a murmur be heard with the second sound, nor could any be

FIG. 6.



John McG. Several occasions after date of Sept. 5th. Late-systolic murmur.

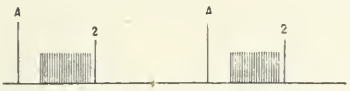
at any time discovered at the aortic cartilage or elsewhere than as described. The man continued to exhibit the symptoms of mitral regurgitation.

CASE III.—The third case, which might even be viewed as a combination of mid- and late-systolic murmur, was seen at my clinic at the Philadelphia Polyclinic during the present year, and the following notes were made:

"April 7, 1892. Sarah J. N., aged forty-seven years, married, has had eight children. She has always enjoyed good health, except for 'typhoid malaria' and for influenza, occurring respectively eleven and two years previously. One year ago she began to suffer from pain in the lumbar region which prevented stooping, and from pain in both lower extremities which extended from the hip to the knees, both in front and behind. There has been no swelling or pain of any joints or any complaint of local tenderness. The pain is not constant and is worse in damp weather. For two months it has been

getting much worse than ever before, and now is so severe at night that she is scarcely able to sleep. She says that she has no palpitation or dyspnœa except on violent exertion, and to no greater degree than a healthy person would experience under similar conditions. Examination discloses no swellings or painful points. The chest is well formed ; the mammæ are quite large and obstruct the inspection of the præcordium. The apex beat is distinctly felt in the fifth interspace within the nipple line. The cardiac dulness is bounded by the third rib and the mid-sternal line. The left border appears to be the nipple line, but the size of the breast interferes with its exact determination.

Fig. 7.



Sarah J. N., April 7, 1892. Combined mid- and late-systolic murmur.

There is no thrill. At the apex the first sound is rather booming and the first portion of the systolic period is unattended by any murmur. At the end of the first third, or perhaps the first half, of the period between the apex beat and the second sound there begins a rather high-pitched, slightly musical murmur, running up to but not replacing the second sound, which is heard distinctly here (Fig. 7). The same murmur, though less loud, and the unaffected first and second sounds are audible at the xyphoid cartilage. Over the base of the heart and of the middle of the sternum the sounds and the murmur are still less distinct. In the axilla the first and second sounds are

Fig. 8.

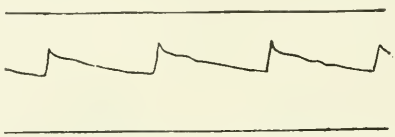
Sarah J. N., April 9, 1892. Bigeminal and alternating cardiac action. Murmur practically the ordinary mitral regurgitant.

quite audible and are clear, and there is a loud murmur of the same character as described. The murmur and sounds are heard very indistinctly at the angle of the scapula. At the aortic cartilage there is a faint first sound, followed by a very faint murmur of the quality and time already described. The second sound is very faint. At the pulmonary cartilage the murmur is faint, and the first and second sounds are likewise faint, though a little louder than at the aortic cartilage. The maximum intensity of the murmur is clearly in the mitral area."

On April 9th the patient was seen again. On this occasion the heart's action was very irregular, and on the slightest exertion, and indeed for the greater part of the time during which the examination was being conducted,

presented a condition of which the following note was made: "The apex beat is very closely followed by the murmur, with an interval very short compared with the condition heard two days ago. The interval is, in fact, so brief that the peculiarity of the murmur could easily be overlooked (Fig. 8). The whole of the systolic period is short, and the murmur is closely followed by a faint but clear second sound. After a short diastole another apex beat occurs which is not attended or followed by any murmur whatever, and after which no

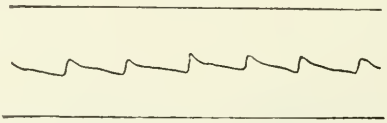
Fig. 9.



Sarah J. N., April 9, 1892. Pulse-beats only one-half as numerous as the ventricular contractions. Murmur that of Fig. 8.

second sound can be heard. The combined time of the second systole and diastole is decidedly longer than the first cardiac cycle. The third cycle resembles the first and the fourth the second. Thus the cardiac rhythm is both bigeminal and alternating, every other ventricular contraction being only sufficient to raise the aortic leaflets a very little as shown by the alternating pulse in the vessels of the neck, but not sufficient to produce any effect in the artery at the wrists, as the sphygmographic tracing shows" (Fig. 9).

Fig. 10.



Sarah J. N., April 9, 1892. Taken when heart exhibited a murmur nearly similar to that of Fig. 7.

After the patient had been at perfect rest for about a half hour she was re-examined and the following condition recorded: "The murmur at the apex is similar to that heard two days ago, except that the interval from the apex beat to the beginning of the murmur is perhaps a little shorter." A sphygmographic tracing was taken while the heart was exhibiting this rhythm (Fig. 10).

The form of murmur just described is certainly very unusual. I have unfortunately not been able to make an extended search through the literature of the subject, but such as I could achieve reveals only occasional and indefinite references to it. I find it alluded to under

the title of "post-systolic" murmur, a name which involves, I think, a misconception of its nature and cause. Gemmill[1] merely refers to the term as being employed by Walshe, Hayden, and others. Walshe,[2] however, simply refers to the existence of a post-systolic murmur, but, so far as I can find, gives no description whatever of it, nor explains how it is produced. It is true that he describes a murmur heard at the *base*, which is abruptly terminated by the second sound, but which he still calls diastolic, and concerning the method of production of which he seems to be uncertain. Hayden[3] reports five instances of "post-systolic" murmur; by which term he designates a murmur occupying the short silence. Only one of these did the author regard as mitral in origin. Bristowe[4] speaks of hæmic murmurs which sometimes occupy only the latter part of the systolic period, and, increasing in force, run into the second sound. They are generally best heard at the junction of the third left costal cartilage with the sternum. These murmurs are not at all similar, therefore, to those now described, and need not be further considered.

The term "post-systolic" could apply to no murmur whatever, except on the theory that the systole of the ventricle lasted only until the beginning of the short silence, and that this silence corresponded to the relaxation of the ventricles and the time supposed to be required for the aortic valve to close. Did this theory represent truly the physiological cardiac rhythm, a murmur heard just before the second sound would be, of course, post-systolic. My own feeling, based only on clinical deductions, and without reference to physiological data, had long been that there existed no pause between the relaxation of the ventricle and the closure of the aortic leaflets long enough to allow of the production of a discernible murmur; *i. e.*, that the closure of the valve was practically simultaneous with the beginning of ventricular relaxation. According to this view the systole begins with the apex beat and lasts to the second sound. This division of the cardiac cycle is, indeed, the one usually accepted, and is that advocated years ago by Volkmann and Donders, who taught that the cessation of contraction of the ventricle and of the streaming of blood into the aorta, the closure of the semi-lunar valve and the occurrence of the second sound were simultaneous. Later studies

[1] Clinical Diagnosis, Finlayson, 1886.
[2] Diseases of the Heart, 1862.
[3] Diseases of the Heart and Aorta, 1875.
[4] Lancet, 1887, ii., 952.

with the cardiograph, however, led various investigators to adopt views differing from this; Landois, Edgren and others placing the second sound after the commencement of the diastolic period. According to these views, and, indeed, according to the scheme for the cardiac cycle as proposed by Volkmann and Donders, it is necessary to admit of the existence of a physiological aortic regurgitation, produced by the blood, in its recoil upon the aortic leaflets, passing backward through the orifice in the process of rapidly closing it. Such an assumption as this seems contrary to the perfection which we have learned to expect in Nature's apparatus. Yet it is evident that if relaxation of the ventricle begins where the aortic valve is widely open, the leaflets cannot be forced together without blood regurgitating at the same time.

The recent careful experiments of Martius,[1] and his exhaustive critical review of the whole matter have thrown great light upon the subject. Martius shows that there is nothing which justifies the assumption of the physiological aortic insufficiency. He claims that after the blood has been expelled from the ventricle into the aorta there is a short period, a "persistence time" (Verharrungszeit), in which the ventricle simply maintains its contracted state. During this time, as Ceradini proved years ago by careful experiments, the semilunar leaflets become closely approximated by a reverse whirl of the blood in the aorta; so that the recoil, when it does come with the first relaxation of the ventricle, finds them in perfect apposition and simply puts them suddenly on the stretch, thus producing the second sound. The existence of this "persistence time" is necessary in order to permit of closure without regurgitation.

This theory, so well sustained by Ceradini's experiments and by Martius's studies of cardiographic tracings, makes the second sound mark the beginning of diastole and the end of systole. It renders absolutely impossible the existence of a murmur just before the second sound, due, as Skoda and others after him maintained, to the friction of the blood on the roughened aortic walls during its recoil upon a competent aortic valve. For the same reason, *i. e.*, that the systole lasts quite to the second sound, the late systolic murmur cannot be accounted for by supposing that a partial aortic regurgitation is taking

[1] Zeitschr. f. klin. Med., xix., H. 1 and 2.

place; the imperfect valves still closing and producing the second sound; for such a murmur would be diastolic in time.

Still another explanation has been advanced for late-systolic murmurs, viz., that regurgitation through a diseased aortic orifice takes place, producing the murmur, and that the pulmonary valve closed a little later than this in time, thus producing the second sound. But this explanation is not very satisfactory, and could by no means apply to cases in which the murmur has the area of diffusion of mitral regurgitation.

Adopting the view that the second sound marks the beginning of diastole, murmurs heard before it must, of course, be systolic. The cases here reported are all instances of systolic murmur heard in the mitral area, and can, with good reason, be regarded as cases of mitral regurgitation. The first two cases not only exhibit the physical signs but the constitutional symptoms of this affection; while the third case, though possessing no subjective symptoms, shows the characteristic area of diffusion, enlargement of the right ventricle, and slight accentuation of the pulmonary second sound; and I unhesitatingly regarded it when seen as an instance of mitral insufficiency. Case I. is an interesting example of what I have called "mid-systolic mitral murmur;" analogous to the mid-diastolic mitral murmur of Bristowe.[1] Case III. and especially Case II. are interesting, in that they offer clinical proofs of the view that the systole lasts quite up to the second sound. The murmur in Case II. ran up so close to the second sound that it at first seemed to replace it. This fact is clinical evidence also that the "persistence time" of Martius must be of exceedingly short duration, as, indeed, the author admits. The very short interval which occurs between the two parts of a double aortic murmur is similar proof of the briefness of this period.

The method of production of mid- and late-systolic murmurs admits of different explanations. If the murmur be at the aortic cartilage an obstructive lesion of the aorta must be presupposed. If it be basic it may be a hæmic murmur, of which the mode of production is not understood. If it be at the apex and with the diffusion of a mitral regurgitant murmur, the existence of insufficiency of the mitral valve may reasonably be assumed. The regurgitation in some

[1] Lancet, 1887, ii.

such cases might depend on no actual valvular lesion. Relaxation of the walls of the ventricle or of the papillary muscles might allow of some slight regurgitation during a portion of the systolic period. It seems much more probable, however, that cases such as those reported are instances of mitral regurgitation of a much greater degree than the murmur alone would indicate. The changes which were noticed at different examinations arouse the suspicion that there existed in all three cases a systolic murmur exactly analogous to the "potential" presystolic murmur described by Bristowe,[1] in which the murmurs heard at different times were but "fitful and accidental roarings of one continuous torrent." The regurgitation, then, in these three cases probably lasted through all, or nearly all, of the systolic period, but usually became audible, for unknown reasons, only toward the middle or latter portions of it.

[1] Loc. cit.

DYSENTERY.

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In this paper we shall attempt to give a general review of those anatomical lesions of the large intestine which are usually grouped together under the name dysentery. The word dysentery is simply a clinical expression, descriptive of diarrhœa, accompanied with pain and tenesmus. It was afterward found that when pain and tenesmus were present in an intestinal flux, the colon, or rectum, or both, were generally the seat of disease, and gradually the word became used in an anatomical sense to express a pathological lesion. Not only do we have various pathological conditions included under this term, but we may have extensive lesions of the large intestine without the clinical symptoms of which the word is expressive. Even in that form of dysentery which from its etiology, the character of its lesions, its symptoms and course, we are justified in regarding as a definite disease due to a definite cause, pain and tenesmus do not form a marked feature in the symptoms.

Our study of the disease is based on 34 cases which have been found in 320 autopsies at the Johns Hopkins Hospital; 305 of these autopsies were made on patients from the hospital, the others were made on cases outside.

When we study the lesions of dysentery from an anatomical point of view we can distinguish various forms which, though they may be more or less associated with one another, present broad and striking points of difference. We have divided them into the simple or catarrhal, the diphtheritic, and the amœbic. The last is distinguished from the others, not only by the anatomical differences in the lesions, but also by the broader difference of a definite etiology.

Diphtheritic dysentery, as the name implies, is characterized by

the presence of a membrane on the surface of the mucous membrane due to a combination of fibrinous exudation and necrosis. It may involve not only the large, but the small intestine as well. It begins with the appearance of small, opaque, whitish-gray masses on the surface of a hyperæmic mucous membrane. These masses cling closely to the surface; they cannot be washed off or removed without the production of a loss of substance. The more elevated portions of the surface, formed by the longitudinal muscular bands and the cross elevations produced by the circular muscular fibres, are the portions most affected. The depressed areas frequently appear as irregular fields of intact mucous membrane in strong contrast to the diphtheritic elevations. These small patches may coalesce, the whole surface may become affected, and the intestine be converted into a dense, rigid tube. In such cases the membrane is usually broken up into small areas, more or less regular in form, by longitudinal and transverse fissures. In other cases there appears to be but little tendency for the areas to coalesce, and the whole surface is thickly covered with small opaque areas, giving an appearance which has been aptly compared to that produced by scattering bran over the surface. The surface is not usually equally affected, and in the same intestine we may find every change from a few scattered spots to a more or less continuous membrane. The process is usually most intense at the bends of the intestine. In the most acute cases the entire intestine is intensely injected and swollen. In other cases there may be no perceptible change in the mucous membrane outside of the diphtheritic areas, and even here the injection may reach only a slight degree.

Sections through the membrane show that it is composed of dense masses of fibrin, necrotic cells, and nuclear detritus. This extends a variable distance into the mucous membrane, or even in some cases into the submucosa. At the bottom it is frequently more or less marked off from the healthy tissue by a line of pus-cells. We can frequently recognize in the necrotic material the remains of glands. The nuclei of the cells do not stain, and the cells themselves are converted into dense refractive masses. The nuclei are broken up, and form the brightly-stained points found in and at the edge of the membrane. Sometimes the membrane is not so sharply limited, and the fibrin extends more or less into the surrounding tissue. The

surrounding mucous membrane is injected, and variable numbers of pus-cells are found between the glands. In the submucous tissue there is intense injection and dilatation of the bloodvessels, which are usually surrounded by a zone of small cell infiltration. In some cases there is an extensive formation of fibrin in the submucous tissue not connected with the membrane on the surface. The fibrin is much more diffuse and has the same fibrillar arrangement as the connective tissue, whereas that on the surface forms a dense reticulum.

Accompanying this process there may be more or less extensive ulceration. The diphtheritic membrane is separated from the surrounding tissue by suppuration, and is cast off, leaving irregular ulcers. When recent they are shallow, and only extend to the area of necrosis. The ulcers may then heal, or the necrosis and fibrinous exudation may extend in the bases of the ulcers. Although the ulceration in diphtheritic dysentery is not usually a prominent feature, it may be so extensive that only small islands of mucous membrane remain. The ulcers are usually shallow and not undermined. The irregularity in the form of the ulcers, especially when they are recent, is a striking feature. Frequently the ulcers appear as fissures, or fissures may radiate from a central ulcer. In very severe and chronic cases the entire wall of the intestine is thickened and contracted. The muscular coat is hypertrophied, and the submucosa in places converted into a dense, hard, cicatricial-like tissue of a slaty color. Even from the peritoneal side we can recognize the process, for the intestine has a dark, slaty color, which does not depend upon change in the mucous membrane, but in the deeper parts. In the more acute cases the inflammation may extend to the peritoneum, as in Case XXXIV., in which there was a fibrinous exudation on the peritoneum, immediately over the portion of the intestine most affected. There is little or no change in the follicles to the naked eye. On microscopic examination they are almost always slightly enlarged, and we may have, along with the diphtheritic lesions, very small follicular ulcers, confined to the surface of the enlarged follicles. This was the form of dysentery found in 11 of our 34 cases. It may appear as an independent affection or associated with a number of other diseases. In the 11 cases it was associated with the following conditions: chronic nephritis, 4; acute nephritis, 1; bronchitis and broncho-pneumonia, 1; amyloid degeneration, 1; cirrhosis of liver,

1; peritonitis, 1; septicæmia, 1; acute diphtheritic gastritis and enteritis, 1.

The descriptions of the lesions in most of the acute epidemics of dysentery conform to this type.

In the epidemic of dysentery in Berne, described by Vogt, most of the cases were diphtheritic. One of the earliest descriptions of it is that given by Cheyne and Osborn in the dysentery prevalent in Ireland in the beginning of this century. It has gradually become to be regarded as the type of dysentery in general. Rokitansky speaks of a necrotic inflammation of the mucous membrane of the uterus as a dysentery of the uterus. It is apparently due to a number of causes. It may be found in poisoning by corrosive sublimate and the mineral acids. Its frequent association with Bright's disease has been supposed to be due to the presence of carbonate of ammonia, which is formed in the intestine, from urea. It is found in a number of infectious diseases, in puerperal fever, in scarlet fever, in smallpox, and in septicæmia. Secondary results do not seem to follow it. In none of our cases was there abscess of the liver. Abscess of the liver seems to be very uncommon in acute dysentery, and does not play any part in the description of epidemics. The slighter forms of diphtheritic dysentery are often an unexpected find at autopsies, and may not be accompanied by any symptoms during life.

We can distinguish from diphtheritic dysentery, catarrhal or simple dysentery. We will have to make this a collective description for those forms which cannot come under the head of diphtheritic or amœbic dysentery. In a catarrhal inflammation of the mucous membrane, according to Virchow, there is increased nutrition of the surface shown in its lighter grades by an increased activity of the secreting cells, and in its higher by suppuration. The suppuration may proceed to ulceration. The name catarrhal is one obviously ill chosen, nor can we recognize an increased functional activity of cells as inflammation.

We can recognize in this a number of conditions and we cannot say that they represent different steps of one and the same process. In certain cases there is a more or less intense hyperæmia of the mucous membrane, which may be general or confined to certain areas; there may be slight punctiform hæmorrhages in the mucous membrane or in the submucosa. The entire mucous membrane may

be more or less swollen and the surface have a dull, grayish appearance. It is often covered with mucus in which there are numerous pus-cells. On microscopic examination of the mucous membrane there is more or less loss of the surface epithelium. The glands are frequently distorted. and the exfoliation of cells extends for some distance into them. They frequently contain pus-cells. The interglandular tissue is thickened and contains pus-cells. Although there may be no loss of substance to the naked eye, microscopic examination will frequently show that there is softening and necrosis extending a variable distance into the mucous membrane. The glands in such places are broken down, their confines lost, and they appear as irregular masses of epithelium surrounded by pus-cells. We may have along with these changes, or without them, more or less extensive ulceration. The ulcers in the most acute form are shallow and never undermined. They are formed by an extension of the superficial suppuration and softening. They may extend into the submucosa, or even to the muscular coat. One of the most typical examples of this form of ulceration is given in Case VII. The mucous membrane of the entire large intestine in this case was hyperæmic and swollen, but the most marked change was immediately around the ulcers; here there was an infiltration with pus-cells most marked just above the muscularis mucosa, and the glands of Lieberkühn showed various degrees of disorganization. All around the ulcers the purulent infiltration extended, in some places down to the muscular coat. The submucous coat was thickened, the vessels hyperæmic and surrounded by masses of granulation and pus-cells. One of the most marked features was the enormous swelling of the connective-tissue cells in the submucosa. They were converted into large, irregularly shaped masses with a large vesicular nucleus. Scattered among the swollen connective-tissue cells there were numerous masses of fibrin. The vessels showed an increase in number and swelling of the endothelial cells. The walls were thickened, and there were numbers of pus-cells both in the vessels and in the walls.

There is nearly always a general involvement of the lymphatic structures of the intestines. Not only is there thickening from hyperplasia of the lymphatic tissue between the glands of Lieberkühn, but the solitary follicles are swollen. At times this swelling of the follicles may be so slight that it is only perceptible on micro-

scopic examination; in other cases they may be two or three millimetres in diameter. The swollen follicles in some cases are grayish and transparent; in others more opaque and white. The swelling is due to a hyperplasia of the lymphatic tissue. Among the lymphocytes there are usually a number of larger epithelioid cells, and there may be some pus-cells present. To the simple swelling of the follicles another change is soon added. The epithelium over the follicles gives way, and a small ulcer is the result. The follicles then appear as elevated nodules with a central depression. We may have the other lesions in the mucous membrane without this change in the follicles, or the follicular change may be so extensive as to mask the others.

This form may become chronic. The ulcers show no tendency to heal. The process of softening and ulceration continues; and we may have large chronic ulcers with hard, indurated bases and thickening of the surrounding tissue. One of the best examples of this is found in Case XXXII. The ulcers in this case were large and deep, with sharp-cut and slightly undermined edges. The base of the ulcer was formed of dense granulation tissue. Most of the ulcers extended only into the submucous coat, but in some the circular muscular coat was also involved, and the cellular infiltration extended between the muscular coats to the peritoneum. The most chronic of these ulcers strongly resembled an ordinary ulcer of the leg. In Case XX. there was a single, large, chronic ulcer of the rectum, and the balance of the intestine showed only a moderate degree of inflammation. In this case there was an abscess of the liver.

We found lesions of this type in fifteen of our thirty-four cases, a little less than half. The number is large, because it includes all the cases not due to amœbæ and without a fibrinous exudation. It was associated with the following conditions: chronic nephritis, 2; carcinoma of stomach, 2; phthisis, 2; general paralysis of insane, 1; abscess of liver, 1; peritonitis, 1; pneumonia and abscess of lung, 1; bronchitis and broncho-pneumonia, 1; carcinoma of tongue, 1; malarial fever, 1; general anæmia, 1; fatty degeneration of heart and kidneys, 1. Of the fifteen cases the condition was chronic in but three. In all the others, the lesions were more or less acute. But two cases (XXX. and XXXI.) of the dysentery of the young

children were examined. In one of these (Case XXX.) there was extensive superficial ulceration which was quite similar in character to that in Case VII. The follicles showed an enlargement only on microscopical examination. In the other, while there was a general diffuse inflammation of the mucous membrane with here and there slight softening of the superficial layers, the ulceration was confined to the follicles. In many of the cases the hyperplasia of the lymphoid tissue, both that of the mucous membrane and the follicles, plays an important part, and the ulceration is secondary to the affection of the follicles. It is probably caused by a simple necrosis of the mucous membrane over the follicles, due to interference with the circulation. The lymph-glands in the meso-colon in the acute cases, both of this and the diphtheritic form, were enlarged, reddened, and softened. In two of the cases, in both of which the disease could be regarded as an independent affection, it was followed by peritonitis in one and abscess of the liver in the other. The character of the abscess was totally different from the more common abscesses following amœbic dysentery.

With regard to the etiology of both the catarrhal and diphtheritic dysentery, we are very much in the dark. In the catarrhal dysentery especially, the lesions are so various that it would not be possible to believe that they could all be due to one distinct cause. In the diphtheritic form, though the lesions may vary greatly in extent, they all have the same essential character. In both forms it is probable that a diminution of the normal resistance of the tissues plays an important part, and this would explain the frequency with which they are met with in the last stages of various diseases.

With regard to the action of bacteria in the production of these forms of dysentery, we know very little. There have been but few observations, and these have not thrown much light on the subject. Ziegler, in his text-book on pathology, has described a small bacillus in cases of epidemic dysentery. It was found both in the exudation and in the mucous membrane. From the constancy of its presence and the relation it bears to the intestinal lesions, he is inclined to regard it as a causative factor. Klebs has also described, in diphtheritic dysentery, a small bacillus, both in the necrotic membranes and in the glands which were separated from the wall. They were also found in the mucous membrane, and in the submucosa, but in very

small numbers. He was enabled to make pure cultures of these bacilli. From his description of the bacilli and the cultures, it seems probable that it was the colon bacillus. We have found similar bacilli in cases both of catarrhal and diphtheritic dysentery. In Case VII. they were especially numerous, both in the ulcers and in the adjoining mucous membrane at the bottom of the glands between the separated epithelial cells and the gland wall. In several places they were also found in the adjoining submucosa. That we do not find similar bacilli, or any, in the normal mucous membrane is of no weight. We know that in any lesion of the intestine, as soon as the protecting epithelium is removed, and the tissue exposed, the colon bacilli can and do enter the tissue, and may be found in the organs. The same might be said of the work of Chantemesse and Widal. They cultivated a small bacillus from the dysenteric stools of five cases of dysentery and from the tissue of the intestine, and from the mesenteric glands and the spleen of a fatal case. By the injection of these cultures into the intestines of guinea-pigs they produced a diphtheritic inflammation of the mucous membrane. Similar bacilli were found there and in the tissues. From the description of the bacilli and cultures in all these cases, it is very probable that the bacillus was the colon.

Case XXX., a child dying while under the care of Dr. Booker at the Thomas Wilson Sanitarium, has been carefully investigated by Dr. Booker, and makes one of the few cases reported in which there have been careful bacteriological examinations of both the stools during life and the intestines a short time after death. The child, twenty months old, suffered from diarrhœa for three weeks before death. The stools were often small, consisting of lumps of mucus and blood, and showing under the microscope chiefly blood-corpuscles and pus-cells, with a comparatively small number of bacteria. The pain at stool was not very marked, and was manifested by restlessness and whining, and not by loud cries. Booker obtained, from cultures at the autopsy from the ileum and colon, numerous colonies of a bacillus which he had not previously met with in the diarrhœal or dysenteric stools of children. The bacillus resembles the bacterium lactis aerogenes in its morphology and growth, but may be distinguished from this by its growth in litmus milk. In the sections of the colon many bacilli were found, which resembled those found in

the cultures, but the colon bacilli were most numerous. Both the colon and the other bacillus, which he calls the new bacillus, were found in the cultures made from the lymph-glands of the colon.

There has recently appeared[1] an article by Ogata in Japan, in which he gives the result of his investigations in an epidemic of dysentery prevailing in one of the provinces of Japan. He examined the bacteria found in the stools of a number of cases, and in tissues taken from one autopsy. Amœbæ were found neither in the stools nor in the ulcers. The short description which he gives makes it possible that the disease may have been amœbic dysentery. The walls of the large intestines were so swollen that the lumen was almost entirely closed. In the mucous membrane of the transverse and descending colon and in the sigmoid flexure of the rectum there were numerous small ulcers. No large ulcers were found. Like Ziegler and Klebs, he describes the organisms as a small, thin bacillus. The bacilli were found in great numbers in the sections of the ulcers, in the mucous membrane, and in the submucous tissue. They were pathogenic for cats, guinea-pigs, and mice. Subcutaneous injections of them in guinea-pigs produced inflammation of the large intestine with ulceration.

Nothing definite as to the nature of the disease can be told from his description.

In Case XXXIV., which was a typical case of acute diphtheritic dysentery accompanying nephritis, a careful bacteriological examination was made of the tissues. Numerous organisms were found in the lesions of the mucous membrane and in the peritoneum over them. In both places the predominant organisms were micrococci, which occurred both in single individuals and in chains. In no case were we able to find organisms which, from their relation to the lesions, we could regard as definitely the cause of them.

The part which the colon bacillus plays in dysentery may be an important one. We know that in nearly all cases in which there is a lesion of the mucous membrane of the intestine, this bacillus is found not only in the seat of the lesion, but in the tissues. The bacillus is pathogenic for a number of the lower animals; and we do not know but that many of the symptoms of dysentery, apart from

[1] Centralblatt. f. Bacteriologie, Bd. xi. No. 9.

those directly referable to the alimentary canal, may be due to these bacilli. It does not seem probable that a bacillus like this, which is constantly present in the alimentary canal, could directly produce lesions of the mucous membrane. But it is not improbable that under certain conditions its virulence could be increased, or, at least, it might be able to act when the resistance of the tissue has in some way been lowered. The occurrence of dysentery in the last stages of numerous diseases speaks somewhat in favor of this view.

When we turn to the third form of dysentery which we have made we find a definite disease, characterized by definite anatomical lesions, and having a definite etiological factor. Eight of the thirty-four cases were of this kind. When we examine the lesions of the mucous membrane in all of these cases we see that although they vary in character in the different cases and even in the same intestine there are certain features in common. The intestine is always considerably thickened, and, although all of the coats are involved in this, the submucous coat is the one most affected. There is not only a general thickening, due to an œdematous condition, but there are sharply circumscribed projecting nodules, in which are small cavities filled with viscid gelatinous pus. There is usually a small opening on the surface leading into these cavities. Frequently these small cavities communicated with one another by means of sinuous tracts which are filled with the same material. The elevated nodules vary in size, and are seated in the submucosa. The openings into them are frequently no larger than the head of a pin or so large that the whole cavity is freely exposed. Even in these cases the surrounding mucous membrane is deeply undermined, and there are often found masses in the submucosa, leading to similar ulcers. These undermined ulcers in connection with the formation of cavities and sinuous tracts in the submucosa may be regarded as the form of ulceration most frequently met with. Ulcers of this character are found in the same intestine with other forms of ulcers. They are most numerous in the last portion of the transverse and descending colon. There are other ulcers with somewhat undermined edges, which represent simply excavations in the thickened submucosa without distinct cavity formation in the tissue, and ulcers which represent a later stage of the excavated ulcer. In these the undermined edges have sloughed away, leaving

the edges in places smooth, in others only slightly undermined. These had a firm base, which generally extended to the muscular coat.

This submucous coat is always the one most affected. This is infiltrated and œdematous, not only in the neighborhood of the ulcers, but in places which are free from ulceration. The ulcers increase in extent by the gradual infiltration and softening of this tissue, with subsequent necrosis of the overlying tissue. The roof which covers in the more or less closed ulcers is broken through, the infiltration and softening continue at the sides, and an ulcer with deeply undermined, ragged edges is formed. The base of these ulcers is clean, and is formed by the muscular coat. Although the ulcer advances in the submucosa by the gradual softening and disintegration of the tissue, the muscular coat offers a barrier to this destruction. The upper layers of it become necrotic, and the cellular infiltration extends through it into the inter-muscular connective tissue septa and subserous coat. Then the same process which took place in the mucous membrane is repeated here. The circular muscular coat is dissected up, the vessels supplying it are destroyed, and it undergoes necrosis. The large sloughs of tissue which are cast off and frequently passed in the stools are composed either of this coat or of the muscularis mucosa. While these processes are taking place the peritoneal coat becomes enormously thickened, and the same process of destruction is continued in this. There are adhesions formed with the surrounding viscera, and the greatly swollen intestine becomes convoluted and adherent to itself and to the surrounding viscera.

The changes in the mucous membrane are for the most part secondary to those in the submucous coat. The ulcers are formed by a continuous advance of infiltration and softening in the submucous and inter-muscular tissue, with necrosis of the overlying tissue. It is possible to divide the ulcers into four forms: (1) Ulcers characterized by cellular infiltration, softening, and cavity-formation in the submucosa; these have a small opening in the mucous membrane and often communicate with neighboring ulcers by passages in the submucosa. (2) Ulcers with slight undermining of the edges, representing simple excavations in the thickened submucous tissue. (3) Ulcers with smooth sides and clean bases. (4) Ulcers with extensive adhering sloughs. Although these various forms at first

sight seem rather different, the differences merely represent different results of the same process. They are due to the nature of the tissue, to its arrangement in layers separated by loose connective tissue, the rapidity of the extension of the process, and probably, in part, to the combined action of other bacteria with the amœbæ.

In all of the cases there was very little change in the mucous membrane at a distance from the ulcers. The covering layer of epithelium was generally absent, and there were slight erosions of the upper part of the glands. Lower down in the mucous membrane some of the glands were dilated and filled with accumulations of mucus and pus-cells. In all of these dilated glands the epithelial cells were filled with mucus, and there seemed to be an increased amount of mucus in the epithelium generally. There was no infiltration of the mucous membrane with leucocytes except in the immediate vicinity of the small glandular cysts which contained them. In some places cysts of considerable size with irregular walls were found, which were probably due to confluence of neighboring glands. At the edges of many of the ulcers, especially those with smooth sides and clean bases, there was marked proliferation of the glandular epithelium. This was shown not only in branching and budding of the glands at the edge, but in a regular epithelial investment of the entire edge of the ulcer, which extended down over the undermined portion, and in some cases partly over the floor of the ulcer. In this new growth of epithelium there were bud-like projections into the tissue beneath, and in some cases these had a lumen and represented newly formed glands. In cases characterized by the formation of cavities in the submucous tissue the roof of the cavity was frequently entirely covered by a new formation of epithelium which had grown downward from the mucous membrane. In most of the ulcers there was not only this proliferation of the epithelium, but the entire mucous surface was folded and turned in over the ulcer.

The submucous tissue around the ulcers is infiltrated with cells. These are in part scattered diffusely through the tissue and partly arranged in masses and rows. The connective-tissue cells are large, pale, and swollen, and in some cases the nuclei do not stain. The processes come out clean and distinct in the homogeneous-looking intercellular tissue. This tissue loses its fibrillation; it is not arranged in bands, but is clear and homogeneous-looking. The cellular

infiltration is most intense in the immediate neighborhood of the ulcers, but there are often masses of pus and round cells separated from the wall of the abscess and lying close beneath the muscularis mucosa.

Amœbæ were first found in the intestinal contents by Lambl in 1849. Losch was the first author who gave an accurate description of a species of amœbæ which he found in the stools of dysenteric patients, together with a careful clinical history and account of the autopsy. This work of Losch is really the pioneer work on the subject, and his description of the organism to which he gave the name of amœbæ coli is so good that but little has since been added to it. The case of Losch's was one of chronic dysentery, with periods of complete remission lasting three years. The lesions in the large intestine were characteristic, consisting of thickening, with extensive undermined ulcers and sloughs. Next to the work of Losch, that of Kartulis in Egypt is the most important. In a series of publications in Virchow's *Archiv* he describes the amœbæ, both in the ulcers in dysentery and in abscesses of the liver accompanying this. In his last paper he reports successful attempts which he made to cultivate them, and claims to have produced dysentery in cats by injecting a pure culture of the amœbæ into the rectum and then tying the anus in order to have the material retained.

Dr. Osler was the first in America to demonstrate the amœbæ. He found them first in the contents of an abscess of the liver, and subsequently in the stools of the same patient. The amœbæ are present in the stools, and may be easily recognized. In searching for them there is some choice in the portion of the stools to be examined. They are rather more numerous in the small, gelatinous masses which are often found in the feces. The numbers of them which are found in the different cases, and even in the same case at different times, vary greatly. At times no single portion of the fæces which can be examined is free from them. In other cases they are only found after a long search. Their numbers in general are proportionate to the severity of the lesions, and they are most abundant in those cases in which the lesions are most acute and most extensive. They may be most easily recognized when moving actively. In an inactive condition they are round and are more refractive than the other cells in the fæces. Their appearance when moving is charac-

teristic. The activity of their motion varies greatly in the different cases, and even in different observations made on the same case. At times the movements are so slow that one must look carefully for some time to make it out, at others the movements are so rapid that certain phases can scarcely be followed. The movement is of two kinds: a progressive movement, and one limited to the protrusion and retraction of pseudopodia. They are from fifteen to twenty-five micro-millimetres in diameter, and we can distinguish in them a slightly granular, refractive interior filled with large vacuoles, and a smooth, homogeneous exterior. The motion seems to take place from the exterior homogeneous substance, the ectosac. A process of this is thrust out, and the interior substance flows into it. Some observers have observed a nucleus in the actively-moving amœba, but we have not been able to distinguish a nucleus from the various vacuoles it contains. It is easy to see the nucleus in sections of tissues which have been hardened in alcohol and stained with safranine.

In the intestine the amœbæ are found in varying numbers in the submucous tissues around the ulcers. They are frequently found in the lymphatics and sometimes in the bloodvessels. Wherever they are present the tissue is swollen, infiltrated with cells, and in some cases there is fibrin formation in the tissue. As a rule, there is no necrosis in the immediate vicinity of the amœbæ; but in a few instances the connective-tissue cells around them have lost their nuclei, and there is some nuclear fragmentation. They were most numerous in the fat of the meso-colon in one case, at the bottom of a deep ulcer which had penetrated into this. As a rule, they are most numerous in the smallest ulcers where the process is rapidly advancing and where there is no suppuration. They are either found simply scattered through the tissue, or they seem to form the advance guard of the cellular infiltration.

It is impossible to say just how the ulcers begin. It is possible that the small glandular cysts in the mucous membrane were the starting-point of the process, but it seems more probable that the amœbæ reach the submucous tissue, producing but few lesions in the mucous membrane, and that the essential lesions are produced in the submucosa, the mucous membrane being attacked from below. So far as can be seen, the changes which they produce in this are œdema with some fibrin formation and necrosis. The œdematous tissue

softens, the mucous membrane is broken through, and the ulcer is formed. The reaction on the part of the tissue is shown, not by the formation of pus, but by the formation of granulation tissue.

In the 33 cases of dysentery, abscess of the liver was found in 7 cases; in 6 of the 8 autopsies of amœbic dysentery; and in 1 of the cases of simple dysentery. In 4 of the cases of amœbic dysentery more than one abscess was found, and in 2 cases they were so numerous and small that they resembled rather multiple tumor metastases than true abscesses. In all of the cases the right lobe was affected, and in 2 cases there were also abscesses in the left lobe. The most common seat of the abscess formation was the right lobe, and there were certain places of predilection in this. They were usually found near the surface, and either in the lower surface of the right lobe, corresponding to the hepatic flexure of the colon, or in the upper surface, close to or within the suspensory ligament.

The contents of these liver abscesses and the character of the wall vary according to the chronicity of the process. On section of the smallest abscess a small amount of glairy, semi-transparent fluid exudes, and leaves behind an irregular, sponge-like mass, the fluid being apparently held in the meshes of this. In the older and larger abscesses the contents are more fluid. The fluid from these has a grayish-opaque color, and suspended in it are more solid masses of tissue. The contents of some of the abscesses were brownish or streaked with brownish-red from admixture with blood. The character of the wall varied. In the smallest and most recent abscesses there was no distinct limiting wall, save the surrounding liver tissue. The larger and more chronic abscesses are lined with a distinct layer of connective tissue, which is sometimes dense and hard, at others soft and œdematous. Even in the same abscess the character of the wall differs. In places it is smooth and fibrous, and at others there were large masses of necrotic tissue, extending from the abscess into the surrounding liver tissue.

On microscopic examination the contents of the abscesses varied. In the smaller abscesses there was fatty granular material, small, irregular masses which could be recognized as fragments of liver-cells and a varying number of pus- or lymphoid-cells. In the larger abscesses the fluid contained a great deal of fat, numerous red blood-corpuscles, fragments of liver-cells, and very few pus-cells. Amœbæ

were found in considerable numbers in the contents of all the abscesses, but they were more numerous in the smaller and more recent abscesses than in the larger and more chronic.

Two distinct sorts of change could be made out in the liver. In all cases, but much more marked in some than in others, there were extensive necroses. These were always more marked in the centre of the lobules than elsewhere. In one case, in all sections examined, the centres of all the lobules for a varying distance around the hepatic vein were necrotic. The necrotic cells have no nuclei, and are converted into irregular refractive masses which stain intensely with eosin and picric acid. In these necrotic areas in the capillaries, and in the necrotic cells, there are numbers of leucocytes. This necrosis is not due to the presence of the amœbæ. There are none found in the liver save in connection with the abscess formation. The action of the amœbæ seems principally shown in the softening and liquefaction of the tissue. The sponge-like tissue in the small abscesses represents the remains of the portal tissue which often formed a more or less connected network, while all the remaining portions were softened and converted into glairy semi-gelatinous fluid. The wall of the abscess was exceedingly irregular, extending wherever the necrotic tissue came in contact with it, and leaving almost intact the portal tissue. The amœbæ were found on sections scattered irregularly through the contents of the abscesses and frequently grouped in numbers around the remains of the portal tissue.

The smaller abscesses do not appear to exert any pressure on the surrounding liver tissue. There is no connective-tissue formation, and the cells, apart from the necrotic changes spoken of, do not undergo any change. In the larger and more chronic abscess there is a more or less distinct wall of connective-tissue which extends to a varying depth into the surrounding tissue. We find in this newly-formed connective-tissue both newly-formed bile-ducts and rows of liver-cells resembling these. The liver-cells for a considerable distance around are converted by pressure into long spindle cells, and bear more resemblance to the spindle cells of a sarcoma than to liver-cells.

Abscess of the lung was found in three of the eight cases. The lower lobe of the right lung was in every case the seat of the

abscess. In two cases the diaphragm was perforated, and the lung abscess was directly continuous with an abscess in the upper surface of the liver. In the other, there was an abscess in the liver, but the diaphragm was intact. The lung abscesses resembled those in the liver in several respects. They were all very similar to each other in their general appearance. All were lined with ragged masses of necrotic material. In every case the tissue adjoining the abscess was firm and solid. Near the abscess it was of a whitish-opaque color, further away it was more grayish and transparent. The consolidation embraced the entire lobe in which the abscess was seated. The consolidation differed from that in croupous pneumonia; the tissue could not be torn; the cut surface was perfectly smooth, and a large amount of fluid could be squeezed from it. Microscopic examination of the abscess contents, or rather of the contents clinging to the wall, for the abscess was generally nearly or entirely empty, revealed much granular detritus, numerous round lymphoid cells, numbers of red corpuscles, pus-cells, and amœbæ. The wall of the abscess is composed of necrotic tissue and a varying amount of connective tissue. As in the liver, in some places this formed a definite wall to the abscess; in others, the wall bordered directly on the lung tissue. The consolidated lung around the abscess offers a perfect picture of interstitial pneumonia. The walls of the alveoli are thickened by connective-tissue formation, which often projects as bud-like masses into the alveoli. The lining epithelium loses its normal characteristics, and it is converted into low cuboidal or cylindrical cells. The alveoli contain as well masses of fibrin, which generally take the form of irregular filamentous masses. Immediately around the abscess the alveoli are often completely filled with large, round, fatty cells. The bronchi in the tissue are much altered. The walls are thickened, and contain great numbers of round cells, and the lumen is often filled with fibrin and pus-cells.

The amœbæ varied greatly in numbers, both in the different cases and in different parts of the same abscess. These were found in the contents of the abscess, and were especially numerous in the places where the abscess is rapidly advancing, and where there is no limiting wall of connective tissue. They are in the greatest numbers in the alveoli immediately adjoining the abscess. They are found in the tissue all around the abscess, but in smaller numbers as

the distance from the abscess increases. They are not found in the bronchi at a distance from the abscess, but in the bronchi near the abscess they are frequently found in considerable numbers. Here they are not only in the wall, but in the lumen as well. In the fibrous wall of the abscess they were found in considerable numbers in some sections, in others they were entirely absent. In this place, as in the corresponding part of the liver abscess, they were either in the bloodvessels or in the spaces of the tissue.

We have given so much space to the description of these lesions because they are those of a definite disease. The lesions which are produced by the amœbæ in the different organs are all the same in kind. They are different from those produced by any bacteria that we know of, and the mode of their production is different. The amœbæ seem to produce both a necrosis of the tissue and a liquefaction of the inter-cellular substance of the connective tissue, as well as of the cells. This action of the amœbæ is seen more clearly in the production of the abscesses in the liver and lungs, where the process is uncomplicated by the action of bacteria, than in the intestine. There is never the remarkable destruction of cells, with the breaking up of nuclei and the formation of nuclear detritus, which is observed in the action of certain bacteria. Nuclear detritus is usually present in a certain degree, especially in the abscesses of the lung, but not necessarily so. The necrotic cells seem to undergo a slow destruction and liquefaction, the nucleus sharing the same fate as the cell protoplasm. In all cases the number of amœbæ found in the lesions bears a distinct relation to the activity of the process. Aside from this direct action of the amœbæ on the tissue we must recognize as probably of equal importance with this the action of the soluble products which they produce, as shown in the diffuse necrosis of the liver cells.

There is no doubt that amœbic dysentery is a common and widespread disease. Numerous cases of it have been reported in Egypt, Europe, and in the United States. In an article published with Dr. Lafleur we went over the most important literature of dysentery with a view to determining the frequency of this form. Both from the clinical and anatomical descriptions of the disease one could be sure of its frequent occurrence, more especially in the description of the disease in the tropics. Chronicity and intermittent character clinically

were associated with thickening and submucous infiltration and sloughing at the autopsy. It is not the acute epidemic dysentery; in that the lesions are distinctly diphtheritic.

The relations of abscess of the liver to this form of dysentery is interesting. The observations of Dr. Lafleur and myself were made on 15 cases, 8 of which died, and in 6 of these there was abscess of the liver. Of course, the statistics from so small a number of cases are unimportant, but the number is a very high one. From the numerous statistics on the relation between dysentery and liver abscess in India, we find about 1 case of liver abscess to $4\frac{1}{2}$ of dysentery; in Algiers, 1 to $5\frac{5}{9}$. Of course, these statistics include all cases of dysentery, and we know that liver abscess is a rare complication of diphtheritic or simple colitis. That it does appear in this, we see from Case XX., in which there was a slight inflammation of the colon and a simple chronic ulcer near the rectum. The abscess in this case differed in a marked degree from the amœbic abscesses. The contents were distinctly purulent, and the wall was that of an ordinary abscess.

The observations both of DeCastro and Kartulis show abscess of the liver to be a common complication of dysentery among the Europeans in Egypt, while Greisinger did not find one case in 186 autopsies of dysentery in native Egyptians. The testimony of all observers is that it is more common among Europeans in the tropics than among the natives. When we turn to the statistics on this subject in Europe and America, the infrequency of liver abscess, as compared with the tropics, is very striking. Rokitansky, in his essay on the dysenteric process, says he has never encountered this complication; nor did Finger find an example of it in the 231 autopsies he made in Prague. Baly did not encounter it in the hundreds of autopsies he made in the Millbank prison. Fyons found only one liver abscess in 51 autopsies of dysentery made in the Crimea. Cheyne found it in 5 out of 30 autopsies in Ireland. The only statistics which we have are those of Woodward and Fox. Woodward found 5 cases of abscess in 90 cases of follicular dysentery, and Fox, in St. Louis, found it 5 times in 30 autopsies of chronic diarrhœa and dysentery.

This much greater frequency of the complication of liver abscess in the tropics than in Europe and America, in what we regard as the

same disease, is inexplicable. Certainly many of the cases described by Finger we would regard as typical of amœbic dysentery. We know—not only from the description of dysentery in Prague, in Vienna, and elsewhere in Germany, but from personal observation—that cases are numerous in which the lesions are those of amœbic dysentery, and yet abscess of the liver accompanying it is a very rare complication. Hlava has found the amœbæ in 60 cases of partly sporadic, partly endemic, dysentery. He says nothing about abscess of the liver, and we presume this was not present in his cases. In Egypt, where the observations of Kartulis were made, and where dysentery ranks as one of the most common diseases, abscess of the liver is certainly more rare than in either India or Algiers. From all reports on the subject we know how rarely abscess of the liver is found in England. When found there, it is usually in sailors who have returned from a voyage to the tropics or in people who have contracted dysentery in India. We have, however, found several cases reported of typical dysenteric abscess in people who have never been out of England.

We think that the following conclusions may be made:

From the various inflammations of the large intestine which form the anatomical lesions of dysentery we can separate one distinct form, both clinically and anatomically, which is produced by amœbic dysentery.

The other inflammations of the colon may appear independently or in the course of other diseases. It is probable that they may be due to a number of causes. It is at present impossible to distinguish in them a characteristic lesion which we can regard as due to the action of a single cause.

Our endeavors both clinically and pathologically should be mainly in the direction of ascertaining whether there are other diseases due to definite etiological factors, the anatomical lesions of which are found among the catarrhal and diphtheritic inflammations of the colon.

Cases.

Case I.—*Class.* Catarrhal. *Associated diseases,* General endarteritis, chronic nephritis. *Anatomical lesions,* Large amount of mucus in the intestine; all of the follicles, particularly those in cæcum and ascending colon, enlarged, and several of them ruptured on the surface forming small ulcers. *Intestinal symptoms,* None.

Case II.—*Class*, Diphtheritic. *Associated diseases*, Acute and chronic endocarditis, chronic Bright's. *Anatomical lesions*, Mucous membrane of descending colon and upper portion of rectum, over a distance of 15 cm. is intensely congested. There are small hemorrhages in the mucous membrane, with adherent fibrinous exudation on the surface. In the cæcum there are small ulcers, with irregular edges, the bases of the ulcers, covered with pseudo-membrane. *Intestinal symptoms*, None.

Case III.—*Class*, Acute diphtheritic. *Associated diseases*, Operation for strangulated hernia; peritonitis, with streptococci. *Anatomical lesions*, All of the follicles in the colon are enlarged. On the surface of many of them, especially near the lower end, there are small erosions of the mucous membrane. Over these places and over the adjoining mucous membrane there is a slight superficial fibrinous exudation. In places the mucous membrane is covered with these minute losses of substance which have a fibrinous exudation, both over and around them. The follicles are prominent in the lower ileum. *Intestinal symptoms*, None.

Case IV.—*Class*, Catarrhal. *Associated diseases*, Chronic endocarditis, chronic diffuse nephritis. *Anatomical lesions*, Mucous membrane of large intestine hyperæmic, and contains much mucus. Throughout its entire length, but most marked in the cæcum, there are small circumscribed elevations from size just visible to the naked eye up to 1½ mm. in diameter. On section they contain a soft whitish mass. They are of a grayish translucent color, and the larger of them are more opaque. The entire cæcum is studded with these small prominences, which are here larger and more opaque than elsewhere. In the small intestine the follicles are slightly enlarged. *Intestinal symptoms*, None.

Case V.—*Class*, Diphtheritic, chronic, and acute. *Associated diseases*, Acute peritonitis from streptococcus infection, catarrhal pneumonia, acute Bright's disease. *Anatomical lesions*, The large intestine is thickened. There are numerous slaty-colored spots in which there are small deep ulcers. On the surface both of mucous membrane and the eroded places there are small patches of whitish fibrinous exudation, which is not easily removed. Most of these patches are no larger than the head of a pin. *Intestinal symptoms*, None.

Case VI.—*Class*, Amœbic. *Associated diseases*, Peritonitis, abscess of the liver. *Anatomical lesions*, The large intestine is adherent to surrounding tissues by fresh adhesions. It is soft and tears easily on attempting to remove it from the body. Its walls are thickened, and it is greatly dilated. The average circumference is 14 cm. There are numerous ulcers and sloughs extending from the cæcum to the anus. In the cæcum there are numerous round elevations, which often communicate with the lumen of the bowel by a small opening. Others apparently have no opening. There are also large irregular ulcers filled with grayish-looking material, on removal of which the muscular coat is seen. In the transverse and descending colon there are large irregular ulcers, covered with partially adherent dark sloughs. On removal of these in some places the transverse muscular coat is laid bare, and in other

places the ulceration extends through this to the longitudinal muscular coat, or to the peritoneum. All of the ulcers, both the large and small, are greatly undermined, and the bases are rough and irregular, and show numerous points of ecchymosis. All the coats of the intestine are thickened and œdematous. There are also elevated ridges leading off from the ulcers and connecting adjoining ulcers. On section these ridges are filled with the same transparent gelatinous material as the ulcers contain. The lymph glands in the mesocolon are slightly enlarged and not softened. *Intestinal symptoms*, Pain in abdomen and diarrhœa.

Case VII.—*Class*, Catarrhal. *Associated diseases*, Carcinoma of the stomach, with metastases. *Anatomical lesions*, There are numerous ulcers in the large intestine, the descending colon and rectum being most affected. The ulcers are generally superficial, and many of them are confined to the mucous membrane. Others are deeper, but none of them extend to the muscular coat. Some of the ulcers are perfectly round; others are of very irregular shape and produced by the union of adjoining ulcers. The edges are smooth and not undermined. In the middle of some of the ulcers there are small portions of intact mucous membrane. The intestine is not thickened except about some of the largest and deepest ulcers. The mucous membrane generally is pale and soft. There are some portions of it more elevated than the rest, which are more opaque and softer. *Intestinal symptoms*, Diarrhœa, with pain and tenesmus two weeks before death.

Case VIII.—*Class*, Amœbic. *Associated diseases*, Abscess of liver. *Anatomical lesions*, The large intestine is contracted. There are numerous ulcers of various shapes and dimensions, which are most numerous in the cæcum and ascending colon. The edges of the ulcers are undermined, and the ulcers generally round or oblong in shape. They contain a grayish gelatinous material, which can be lifted from the base of the ulcer and from beneath the overhanging edges. In the transverse colon the ulcers are larger. In one place the floor of the ulcer is formed by the longitudinal muscular tissue. Some of the smaller ulcers project above the surface and communicate with one another by fistulous tracts in the submucosa. *Intestinal symptoms*, Diarrhœa, with pain and tenesmus.

Case IX.—*Class*, Diphtheritic. *Associated diseases*, Chronic nephritis, membranous enteritis. *Anatomical lesions*, The large intestine is dilated, its walls thin. Scattered over the mucous membrane there are numerous serpiginous erosions and shallow ulcerations, covered with fibrinous exudation. This condition is most marked in the cæcum and ascending colon. The mucous membrane of the rectum contains shallow ulcers, with here and there intense injection of the eroded surface. Mucous membrane of small intestine is opaque and slightly yellowish. This appears due to a superimposed layer of material which can be scraped off in slightly adherent masses, but which does not wash away. In this there are numerous irregular fissures, which are slightly stained with bile. *Intestinal symptoms*, Diarrhœa, with pain and tenesmus for past year, alternating with periods of constipation.

Case X.—*Class*, Amœbic. *Associated diseases*, Peritonitis, abscess of liver

and lung, *Anatomical lesions*, The colon is free from adhesions except at two places, where it is firmly adherent to the stomach. It contains intensely fetid soft brownish contents. There are numerous ulcerations which are most extensive in the cæcum and ascending colon. Here there are large areas entirely devoid of mucous membrane, with a firm base extending to the muscular coat. The mucous membrane adjoining these is hyperæmic and undermined. In the transverse colon there are much deeper ulcers—one penetrating into the fat of the mesocolon, and one passing entirely through to the adherent peritoneum. The entire colon is greatly thickened. The ileum for 12 cm. above the valve contains ulcers of the same character as the colon. *Intestinal symptoms*, Intermittent diarrhœa, stools yellowish-brown, contain no blood.

Case XI.—*Class*, Catarrhal. *Associated diseases*, General paralysis of insane. *Anatomical lesions*, The large intestine contains numerous hard balls of fecal matter. The entire surface, but especially the ascending colon, is covered with a firm white layer of mucus, which cannot be washed off, but can be pulled in small adherent strips. In the cæcum there is a small polypus, the extremity of which is necrotic. *Intestinal symptoms*, None.

Case XII.—*Class*, Amœbic. *Anatomical lesions*, There is more or less extensive ulceration throughout the large intestine. It is least marked in the transverse colon, but everywhere else the bowel is riddled with ulcers. The mucous membrane, where intact, has a grayish-red color, deepening to a chocolate-brown. There is nowhere any necrosis or fibrinous exudation on the surface. The ulcers are very irregular in shape; they run into one another, and are either clean or covered with a thin granular-looking pellicle of a grayish color. They often reach the muscular coat, but do not penetrate it. Their edges are greatly undermined. In the transverse colon there are only a few widely separated ulcers, and between these the mucous membrane is healthy. In the cæcum the ulcers are shallower than in the other parts of the intestine. The submucous coat in the vicinity of the ulcers is greatly thickened. In the lower portion of the ileum there is a diphtheritic inflammation. *Intestinal symptoms*, Irregular diarrhœa.

Case XIII.—*Class*, Amœbic. *Associated diseases*, Abscess of liver and lung. *Anatomical lesions*, The large intestine shows numerous ulcers, which are especially marked in the transverse and descending colon. These ulcers are sharply circumscribed and of various shapes, with the long axis generally transverse to the intestine. Most of them extend to the muscular coat, and in some cases into this. The edges of all are greatly undermined. Several of the ulcers extend through the transverse muscular coat, which is dissected up for a short distance around the ulcer. *Intestinal symptoms*, Acute diarrhœa, with pain and tenesmus.

Case XIV.—*Class*, Amœbic. *Associated diseases*, Peritonitis. *Anatomical lesions*, The large intestine is very much thickened. There is also extensive ulceration, the ulcers varying greatly in character and extent. In the lower portion of the descending colon there are small ulcers, with undermined edges filled with viscid, transparent pus. In the upper portion of descending colon there are larger ulcers, with deeply undermined edges, and a clean base extend-

ing down to the muscular coat. The undermined edges are filled with gelatinous pus, and some of the ulcers are connected with one another by sinuous tracts in the swollen submucosa. In the transverse colon there is a large loss of substance, 8 cm. in length. It is partly covered by a large mass of dark brownish necrotic material, which is attached to one side of the ulcer. This large slough is composed of the circular muscular coat. The base of the ulcer is principally formed by the thickened peritoneum. At the hepatic flexure, and partly covered in by adhesions, there is a large opening, 10 x 3 cm. The wall of the gut here is formed partly by the adherent ileum and partly by a necrotic slough of the muscular coat, which adheres along one edge of the ulcer. In the rectum there are also extensive ulcers covered with sloughs. *Intestinal symptoms*, Diarrhœa, with pain and tenesmus.

Case XV.—*Class*, Amœbic. *Associated diseases*, Abscess of liver perforating into duodenum, peritonitis. *Anatomical lesions*, There are numerous adhesions about the colon. It is dilated and thickened, and contains a large amount of soft yellowish-brown material. In this material there are small white translucent masses, which do not mingle with the other contents, and can be lifted out entire. The mucous membrane is pale-grayish, œdematous looking, and there are numerous ulcers of various size, particularly in the ascending and transverse colon. These ulcers have ragged undermined edges, and extend down to and into the muscular coat. Betweeen the ulcers there are numerous elevations on the surface, some of these round, others long and irregular. In most of them there is a small opening on the apex leading into a small cavity filled with viscid gelatinous material. Many of these cavities communicate with one another by fistulous tracts in the submucosa. Some of these tracts are from 2 to 5 cm. long. *Intestinal symptoms*, Diarrhœa from beginning of illness, soft stools containing blood and necrotic material.

Case XVI.—*Class*, Amœbic. *Associated diseases*, Abscess of liver and lung. *Anatomical lesions*, The entire large intestine is dilated, thickened, and covered with numerous ulcers. In the intestine there is a thin brownish material. The ulcers have irregular shapes, with wide overhanging edges. The smaller contain viscid translucent material, which can be lifted as a mass from the cavity. Most of the ulcers extend only to the transverse muscular coat. Others pass through this, and the base is formed by the thickened peritoneum. The transverse colon is most affected. In this the ulcers occupy large areas, with only small masses of mucous membrane separating them. The bases of some of the larger ulcers are imperfectly divided by septa, showing that they were formed by the confluence of several. *Intestinal symptoms*, Intermittent diarrhœa, soft, brownish stools.

Case XVII.—*Class*, Diphtheritic. *Associated diseases*, Bronchitis and broncho-pneumonia. *Anatomical lesions*, The large intestine in several places is doubled or folded on itself, and there are adhesions between these and with the surrounding viscera. The mesocolon is thickened and hyperæmic, and the glands in this enlarged and reddened. The intestine is firm and thickened. There are extensive ulcerations, which are most marked and deepest in the descending colon and rectum. They are generally superficial, only a few ex-

tending to the muscular coat. The bases are firm and indurated, partly covered with an adherent fibrinous exudation. The edges are sharp and not undermined. In the lower colon and rectum, where the ulceration is most extensive, there are only small islands of intact mucous membrane. In the transverse colon there are several large superficial ulcers with smooth edges. The bases of all of these are hard and covered with a slight adherent fibrinous exudation. *Intestinal symptoms*, Illness began two weeks before death ; diarrhœa with tenesmus.

Case XVIII.—*Class*, Diphtheritic. *Associated diseases*, Pelvic peritonitis, amyloid infiltration. *Anatomical lesions*, In the cæcum there are numerous small irregular erosions of the mucous membrane. They are most numerous and extensive in the descending colon and rectum. The edges of the erosions are sharp and not undermined, the bases generally clean, but here and there a small amount of fibrinous exudation is seen on the surface. The submucosa beneath and about the ulcers is thickened and infiltrated with pus. *Intestinal symptoms*, Diarrhœa for past five or six months, with pain and tenesmus; stools very frequent, and often contain blood and mucus.

Case XIX.—*Class*, Diphtheritic. *Associated diseases*, Chronic diffuse nephritis. *Anatomical lesions*, The large intestine is thickened and surrounded with dense masses of fat. The mucous membrane is absent over almost the entire ascending and transverse colon. Only here and there small areas of intact mucous membrane are seen. In the splenic end of the transverse colon and in the descending colon there are smooth shallow ulcers, with indurated margins. Everywhere in and about these ulcers there is a closely adherent diphtheritic deposit. *Intestinal symptoms*, Eighteen days before death, diarrhœa with some blood in stools.

Case XX.—*Class*, Catarrhal. *Associated diseases*, Abscess of liver. *Anatomical lesions*, The follicles in the lower end of the ileum and in the entire large intestine are enlarged. The mucous membrane of the large intestine is thickened and hyperæmic. In the rectum, 6 cm. from the anus, there is a round ulcer 14 mm. in diameter. Its edges are smooth and slightly undermined, its base clean and soft. *Intestinal symptoms*, No diarrhœa.

Case XXI.—*Class*, Catarrhal. *Associated diseases*, Phthisis. *Anatomical lesions*, In the lower end of the ileum and in the entire large intestine the follicles are swollen. The mucous membrane of the large intestine hyperæmic, swollen, and there are small erosions, generally not involving the entire thickness of the mucous membrane, and chiefly on the surfaces of the swollen follicles. *Intestinal symptoms*, Diarrhœa four weeks before death, with some abdominal pain.

Case XXII.—*Class*, Catarrhal. *Associated diseases*, Peritonitis. *Anatomical lesions*, The entire large intestine is thickened and somewhat dilated. The entire surface is firm and of a slaty color. In this there are numerous rather superficial losses of substance, with firm smooth edges and a slaty indurated base. The mucous membrane has areas of hyperæmia. *Intestinal symptoms*, Diarrhœa lasting three months, followed by ascites, which began seven weeks before death.

Case XXIII.—*Class*, Catarrhal. *Associated diseases*, Death one month after operation for carcinoma of breast; pneumonia and abscess of lung, acute pleurisy. *Anatomical lesions*, The large intestine somewhat dilated, and contains soft black masses of feces. The entire mucous membrane is hyperæmic. In the descending colon there are numerous shallow ulcers. The rectum contains numerous large ulcers, with soft, reddened, elevated edges. *Intestinal symptoms*, Diarrhœa commenced on day of operation, and continued until death.

Case XXIV.—*Class*, Diphtheritic. *Associated diseases*, Arterio-sclerosis, diphtheritic gastritis, and enteritis. *Anatomical lesions*, The mucous membrane of the stomach is reddened in places, and presents chiefly along the greater curvature a thin superficial diphtheritic exudation of a dirty yellowish-white color, adherent to the mucosa and consisting apparently of a superficial necrosis of the mucous membrane. It occupies several patches 2 to 3 cm. in length. In the small intestine there is an intense diphtheritic enteritis involving the entire length of the jejunum and ileum, and most intense in the lower end of the ileum. The mucous membrane is coated with a superficial dirty brownish, firm necrotic layer. All of the coats of the intestine are of a dark red color and soft consistency. In the colon the process is more intense than in the ileum and more in patches. The mucous membrane is coated with a thick opaque yellowish diphtheritic layer, and in many places has a rough or rugous surface, caused by elevated and depressed parts. There are no actual ulcerations. The diphtheritic process extends to the rectum, but is not more intense in one part than in another. *Intestinal symptoms*, Ten days before death began to complain of diarrhœa, which resisted ordinary treatment; stools very frequent, containing at times blood.

Case XXV.—*Class*, Catarrhal. *Associated diseases*, Bronchitis, bronchopneumonia, interstitial pneumonia. *Anatomical lesions*, The mucous membrane of the colon is intensely hyperæmic and thickened. Here and there over the surface there are small superficial erosions. *Intestinal symptoms*, Pain in abdomen, and diarrhœa with tenesmus; twenty to thirty dark liquid stools daily.

Case XXVI.—*Class*, Diphtheritic. *Associated diseases*, Gangrenous inflammation of penis, septicæmia, anæmia. *Anatomical lesions*, The colon contains soft yellowish fæces, which are firmer in the rectum. The solitary follicles are swollen, and some of them are as large as split peas. Many have yellowish, apparently necrotic, centres, or even a bit of yellowish membranous material adherent to them. In some places the swollen follicles have a central loss of substance, producing small follicular crater-like ulcers. *Intestinal symptoms*, None.

Case XXVII.—*Class*, Catarrhal. *Associated diseases*, Malarial fever, bronchitis. *Anatomical lesions*, The rectum contains hard yellowish scybalæ coated with mucus. Similar balls of feces also in colon and cæcum. The mucous membrane of large intestine, particularly in the sigmoid flexure and colon, is coated with firmly adherent, stringy, tenacious, white mucus, often peculiarly arranged in anastomosing lines. The mucus is of about the con-

sistency observed in the discharges in cases of mucus or membranous diarrhœa. *Intestinal symptoms*, None.

Case XXVIII.—*Class*, Catarrhal. *Associated diseases*, Œdema of glottis following removal of tongue for carcinoma. *Anatomical lesions*, The follicles in the entire large intestine are moderately swollen. Mucous membrane hyperæmic. *Intestinal symptoms*, None.

Case XXIX.—*Class*, Catarrhal. *Associated diseases*, Carcinoma of stomach, with mestastases. *Anatomical lesions*, The mucous membrane of the large intestine is hyperæmic. All of the solitary follicles are enlarged, white, opaque, and appear prominent against the dark color of the mucous membrane. *Intestinal symptoms*, None.

Case XXX.—*Class*, Catarrhal. *Associated diseases*, Anæmia. *Anatomical lesions*, The entire length of large intestine, from the cæcum to the anus, is extensively ulcerated. The ulceration is generally superficial, involving not more than the mucous membrane. The ulcerated part has a smooth grayish appearance, with irregular margins. The remaining mucous membrane standing as islands, and larger and smaller areas, on this grayish ulcerated surface. These portions of mucous membrane are highly congested, swollen, brownish-red and velvety. [At first glance it is not altogether easy to say whether there is any ulceration except the small ones, but frozen sections show the ulceration to be so extensive in places, for instance, just above the anus, that only here and there a small islet of mucous membrane remains.] There is no undermining of the mucous membrane. The process involves the whole large intestine with about equal intensity. Perhaps rather more intense in the lower part. In the superficial ulcerated portions there are small, round, deeper ulcers, generally not more than 2 to 3 mm. in diameter, which can be easily recognized as ulcers. *Intestinal symptoms*, Diarrhœa, with slight pain.

Case XXXI.—*Class*, Catarrhal. *Associated diseases*, Fatty degeneration of heart and kidneys. *Anatomical lesions*, In the splenic flexure and descending colon there is a large area, 7 cm. long, of deep injection of the entire circumference of bowel. There is some mucus and blood in the lumen of the intestine. At this place, and in the entire descending colon, the solitary follicles are swollen and injected. In some of them there is a slight depressed loss of substance in the centre. The mucous membrane between the follicles and ulcers is swollen, soft and injected. *Intestinal symptoms*, Diarrhœa, with bloody mucous stools.

Case XXXII.—*Class*, Catarrhal. *Associated diseases*, Phthisis. *Anatomical lesions*, Mucous membrane of ascending colon normal. Commencing at the end of the transverse colon there is extensive ulceration. The ulcers cover almost the entire extent of the gut, and between them there are only small areas of mucous membrane. They extend along the gut for a distance of 45 cm. The ulcers are deep, irregular in shape, the adjacent mucous membrane thickened and slightly overhanging the ulcers. The bases of ulcers are firm, pale, and covered with irregular granules. In the lower half of rectum the mucous membrane is entirely absent, with the exception of a small fold just above the anus. The mesenteric glands are not enlarged. There is no

appearance of caseation or tubercles in the bases of the ulcer nor in the thickened peritoneum over them. *Intestinal symptoms*, Diarrhœa.

Case XXXIII.—*Class*, Diphtheritic. *Associated diseases*, Cirrhosis of liver, fibrinous peritonitis, ascites. *Anatomical lesions*, The large intestine is the seat of superficial patches of diphtheritic ulceration, most intense in rectum, extending half way up colon, disappearing in ascending colon. Mucous membrane of rectum very much reddened and hæmorrhagic, with round, oval, and irregular superficial ulcerations. They do not extend through the entire mucosa, and are covered with a thin, gray, diphtheritic exudation on a hemorrhagic base. There are also flat projections of a grayish-red color, covered with a thin grayish-brown exudation. The ulceration is very superficial. Higher up the ulcers are less numerous and more regularly round and oval, measuring from $\frac{1}{2}$ to 1 cm. in diameter. The non-ulcerated elevated patches of diphtheritic exudation are more numerous than in rectum. *Intestinal symptoms*, Diarrhœa.

Case XXXIV.—*Class*, Diphtheritic. *Associated diseases*, Chronic nephritis, tuberculosis. *Anatomical lesions*, In the last part of the descending colon and rectum there are numerous ulcers. These are superficial, with well defined edges. Their base is rough and irregular, and covered with a dirty grayish diphtheritic exudation. Most of the ulcers have their long axis transverse to the intestine. The mucous membrane around the ulcers is distinctly hemorrhagic. The ulceration extends almost to the middle of the descending colon, gradually becoming less intense. At this portion the ulcers are almost circular, with clean sharp cut edges and a diphtheritic base. There are also ulcers which represent only superficial erosions of mucous membrane, and which are without any fibrinous exudation. *Intestinal symptoms*, Diarrhœa, with slight pain.

THE SYMPTOMS, COMPLICATIONS, AND TREATMENT OF DYSENTERY.

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In continuing the discussion on dysentery, begun by Dr. Councilman's paper on the etiology and pathology, I shall be obliged to limit myself, in the part assigned to me, to certain points rather than attempt a complete treatment of it, as this would be impracticable within the limits of this paper.

In the literature of dysentery, even in that of quite recent years, nothing is more noticeable than the lack of any agreement as to the meaning of the term. By many writers dysentery is still regarded as a morbid entity, an infectious disease expressing itself by an inflammation of the large intestine, essentially the same in its sporadic, endemic, and epidemic forms, in tropical climates and northern latitudes, and varying in its symptomatology and pathology in different cases only in accordance with climatic and other modifying conditions. Other writers, although insisting upon its infectious character, admit a variety of infectious causes, while still others broaden the term into a generic expression for a group of inflammations of the large intestine that are partly of specific and partly of non-specific origin; the latter view is the one here adopted, and is the only one permissible with our present knowledge. It is no longer possible to speak of dysentery as we do of typhoid fever or Asiatic cholera. There is no single pathological entity to which the term belongs exclusively, and, if we are to retain it, we can do so only in the sense in which we use the word pneumonia—that is, as a convenient name for a number of affections implicating a particular organ and having certain more or less typical symptoms in common.

Of the various classifications of dysentery that have been proposed, the division into four groups, viz., catarrhal, diphtheritic, amœbic,

and secondary dysenteries, although open to the objection of being partly anatomical and partly etiological, is probably the most serviceable one, as these forms can be differentiated from each other during life by their symptoms with a considerable degree of certainty.

Symptomatology.

Acute Catarrhal Dysentery. The form most common in sporadic cases. The access of symptoms, although occasionally sudden, is usually gradual, is rarely initiated by a chill, and the dysenteric symptoms are preceded by a diarrhœa of one or more days' duration. There is usually some fever, the amount depending chiefly on the extent of the catarrhal process, and rarely reaching a high grade. The stools, at first fecal with some mucus, soon change to small, frequent discharges of a mixture of mucus and blood, later with the addition of pus and detritus from the surface of the mucous membrane and the occasional passage of scybala, and accompanied by tenesmus and tormina. Vesical tenesmus, retention of urine, and prolapsus ani are rarely present in this form. The frequency of the discharges, greatest in the first few days, decreases afterward with a uniformity that is more or less characteristic, and at the same time there is a restoration of the function of the intestine as shown by the reappearance of fecal stools. The discharges have usually but little offensive odor, and contain no sloughs of the mucous membrane. The milder cases terminate in a week or ten days even without treatment, the more serious ones may be protracted to three or four weeks. The catarrhal process shows but little tendency to become chronic, and is rarely accompanied or followed by the more serious complications of dysentery.

Acute Diphtheritic Dysentery. Here the symptoms are of a graver type. Some of the cases begin apparently as catarrhal dysentery, and after a few days' illness a marked aggravation of the symptoms occurs, with tenderness over the colon, extreme thirst, dry tongue, and delirium. In other instances the attack begins suddenly with a chill, and severe prostration is present from the start. The stools vary in character with the site of the lesion, and are more commonly watery than in catarrhal dysentery. The mucus or mucopus is mingled with or replaced by a thin reddish serum in which float

yellowish or reddish morsels—the necrosed fragments of the diphtheritic layer—the discharges resembling meat washings (lotura carnea), and having a pronounced cadaveric odor. Later, necrosed portions of the mucosa, sometimes of considerable size, and even entire casts of the intestine, may be discharged. The stools are then of a brownish or blackish color, and horribly offensive. The temperature is usually higher than in catarrhal dysentery, at least at the outset, but in adynamic states it may be normal or subnormal, while some cases run their entire course without fever. Tormina, rectal and vesical tenesmus, and retention of urine are usually more conspicuous symptoms than in catarrhal dysentery, but in some cases may be entirely absent. The duration is usually from one to four weeks.

Amœbic Dysentery. The following sketch of the symptoms of this form are taken in abstract from the excellent description given by Councilman and Lafleur(1) in their monograph on this affection, as I have had no opportunity of studying the disease myself, except in one case now under observation in the New York Hospital.

The attack may begin either acutely or gradually. If acutely, there is at first a watery diarrhœa followed by frequent bloody and mucous stools with tenesmus and tormina, or dysenteric stools may be present from the start. In cases of gradual development the symptoms are rather those of diarrhœa than of typical dysentery. The stools are not very frequent, watery, with more or less mucus and blood or with none at all, and the diarrhœa is interrupted from time to time by short periods of constipation. In either form there is usually no fever, except when diphtheritic inflammation is superadded, or secondary abscesses develop in the liver or lungs. In gangrenous cases the same adynamic symptoms and putrid stools with fragments of necrosed tissue are observed which we have noted in diphtheritic colitis. Perhaps the most distinguishing feature of this form of dysentery is the absence of the uniformity in the movement of symptoms that belongs to the catarrhal and diphtheritic varieties. In most cases there are periods of intermission followed by acute exacerbations that sometimes resemble a primary attack, while similar but less marked fluctuations may occur even in the gangrenous cases. Convalescence, which is usually slow, is apt to be interrupted from time to time by slighter recrudescences of diarrhœa with reappearance of amœbæ in the stools. The average duration is much longer than

in either of the other forms, varying from two weeks to several weeks or months or years; in fact, amœbic dysentery is characterized by a marked tendency to chronicity.

The stools all contain "more or less numerous, small, opaque or translucent, gelatinous, grayish-yellow masses 1–3 mm. in diameter," floating in the liquid or clinging to the formed movements in intermissions of the diarrhœa. Amœbæ are found in all varieties of the discharges, being most numerous in the severe acute cases, in the periods of exacerbation, and in the gelatinous masses; less frequent in the fluid portions of the stools and in the necrotic fragments. During convalescence the amœbæ gradually decrease in number, but may still be found at times even after the movements appear normal. As the amœbæ lose their characteristic motility and disappear wholly or in part from stools that have acquired an acid reaction (Cunningham(2), movements which are to be examined should be passed into a warm bedpan kept at a temperature of 30° to 35° C., and the microscopical examination made at the earliest practical moment. Generally a single examination is sufficient, but several may be required when the stools contain but little mucus.

Secondary Dysentery. In this form, which may develop during the course of any severe constitutional disease, "dysenteric" symptoms are almost always absent, and the existence of colitis is rarely suspected during life. There is usually only a slight uncharacteristic diarrhœa—a few loose movements daily during the terminal stages of the primary disease. In an instance of this kind which came under my observation during the past winter in a case of pyelitis, the patient had three or four loose movements daily for ten days before his death, without tormina or tenesmus and with only occasional traces of mucus, or blood. At the autopsy the colon was found riddled with ulcers, one of which had perforated the bowel near the sigmoid flexure, where a small abscess had formed. There was no peritonitis or lesion of the small intestine.

This absence of "dysenteric" symptoms, which is the rule in secondary colitis, is by no means very infrequent in the other forms of dysentery, and it is not easy to understand how a writer with so large a clinical experience as Trousseau(3) could have made the statement that "tenesmus of an exceedingly painful nature is an essential characteristic of dysentery." Woodward(4), in collating the cases of

intestinal flux reported during the Civil War, excluded from the category of dysentery all cases which did not at some time in their history present this symptom, but he adopted this rule merely as the only practical method, in the absence of satisfactory clinical reports, of separating the dysenteric from the diarrhœal fluxes. There is abundant evidence that in both sporadic and epidemic dysentery the stools may be of a diarrhœal character during the entire course of the attack, and that tormina and tenesmus may be altogether absent or play but an insignificant part. In a recent severe epidemic at Columbia, Louisiana, which was characterized by extraordinary vital depression, and in which the mortality was 80 per cent. at the height of the epidemic and 40 per cent. in its decline, Dr. Wright(5) reports that tormina and tenesmus were "conspicuous only by their almost entire absence." In the very fatal epidemic in the Cumberland and Westmoreland Asylum, England, with twenty deaths out of thirty-one cases, and which was apparently due to effluvia from a field irrigated by sewage, Dr. Clouston(6) had the same experience in some of the cases. Fagge(7) states that he has seen "two well-marked instances of fatal sporadic dysentery occurring in London, in each of which there was a very extensive diffused ulceration of the large intestine, the presence of which had been entirely unsuspected during life." This absence of typical symptoms is commonly due to localization of the lesions in the upper parts of the colon, but it is noticed occasionally in adynamic cases with implication of the entire colon, and seems to be specially frequent in amœbic dysentery. When the upper colon and the lower ileum are alone involved, the character of the stools and the general course of the symptoms may easily lead to a diagnosis of typhoid fever.

Few inflammatory affections are characterized by so rapidly developing an anæmia as acute colitis. Even in cases of moderate severity, with little or no fever, and terminating, so far as the intestinal symptoms are concerned, in one or two weeks, the disturbances of nutrition are usually sufficiently serious to render the convalescence more or less protracted. Niemeyer(8) says that he has seen general anæmic dropsy ensue more frequently after mild attacks of dysentery than after any other disease of equally short duration. This tendency to anæmia is favored, doubtless, by the losses of albumin and blood in the stools, but the importance of this factor has

been exaggerated by some writers. A more satisfactory explanation is to be found in the marked derangements of the digestive functions. Uffelmann(9) has shown that in all but the mildest cases the saliva becomes acid, loses its saccharizing properties, and contains much less than the normal number of salivary corpuscles, and that the gastric juice is either less acid than is normal or becomes alkaline with loss of peptonizing power. The biliary secretion is usually much diminished, or it may be almost completely arrested for several days, as in Uffelmann's case of dysentery in a woman with a biliary fistula, or there may be hypersecretion of bile with nausea and greenish vomiting. Similar derangements probably occur also on the part of the pancreas and glands of the small intestine, but upon this point we have no direct evidence. To these causes of anæmia may be added the destructive influence of septic organisms or their ptomaine products on the blood cells.

Complications.

In considering the complications of dysentery I shall omit hepatic and hepato-pulmonary abscesses, as their symptoms and treatment will be considered by Dr. Dabney in his paper on hepatic abscess.

Malarial Complications. The old doctrine that dysentery can be caused by the same infection that produces malarial fevers is abandoned by recent authorities, and yet Aitken(10), although he does not claim the identity of the two infections, says that the "connection is so intimate that a given number of persons being exposed to the action of paludal miasmata—as, for example, a boat's crew sent ashore in a tropical climate—the probabilities are that of the men returning on board part will be seized with dysentery and part with intermittent fever." But admitting the fact, it by no means proves any intimate connection between malarial fever and dysentery. Such an incident might happen very readily in localties where both diseases were prevalent at the same time, but it could not occur in other numerous tropical regions where one disease not infrequently exists as a severe endemic to the entire exclusion of the other. Hirsch(11). The frequent coëxistence of the two infections in the same individual is, however, quite another matter, and one about which there is no dispute. There is ample evidence that malarial infection not only predisposes to dysentery, but may aggravate its symptoms and pro-

long their duration. In its severer forms malarial intoxication at times determines congestion of all the abdominal viscera, including the intestinal canal, where it may excite a catarrhal condition of both the small and the large intestine. The course of dysentery may be modified materially, therefore, particularly in tropical climates by this complication, but the diagnosis of it is attended by certain difficulties, and is doubtless often made upon insufficient grounds. Maclean(12) says that the malarial element may be "recognized by the periodicity of the febrile paroxysms, the presence of gastric irritability such as we see in remittent fevers, and by the peculiarity of the evacuations, which from the first are serous and contain but little blood, but have the characteristic odor." Other writers mention also a periodicity in the frequency of the stools, while the occurrence of chills is very commonly regarded as of malarial significance.

All of this evidence is by itself inconclusive. Fever of a more or less remittent type, pronounced gastric symptoms, diarrhœal rather than typical dysenteric stools, and even a certain periodicity of the intestinal flux, are all symptoms that are met with in the dysentery of regions where a malarial element can be excluded, while chills are frequently only indications of septic processes in the liver or elsewhere. Before resorting to the experimental test with quinine, other evidence should be sought for in the history of a previous malarial infection, in the presence of an enlarged spleen palpable below the free border of the ribs, and in the detection of the plasmodium malariæ in the blood.

Dysenteric Arthropathies. Since Sydenham's(13) allusion to the occurrence of joint symptoms in an epidemic of dysentery in 1672, this complication has been observed in numerous epidemics and occasionally in sporadic cases. A recent interesting study of it by Dewevre(14) gives the results of his compilation of 65 cases, 15 of which occurred among the 445 cases of dysentery under his care in the Military Hospital at Lyons, France, during the summer of 1885.

The onset of articular symptoms occurs at variable periods of the dysenteric attack. Out of 60 observations in which the date of invasion was mentioned, in nine it fell in the first week, in seven in the second, and in forty-four in the first days of convalescence, or several weeks later. Occasionally the development of the arthro-

pathy is preceded by a sudden arrest of intestinal symptoms, or the course of the joint lesion is interrupted by reappearance of the flux. In one of the reported cases this alteration of articular and intestinal symptoms recurred three times in the same individual. The invasion is always sudden, and at first affects but a single joint. Out of sixty-three cases the attack began in the knees twenty-five times, in the ankles sixteen times, in the shoulders nine times, in the elbow four times, in the hip once, in the right middle finger once, in the toe of the left foot once, in the temporo-maxillary articulation once, and once in the sterno-clavicular articulation.

The symptoms are of slight intensity. There is but little pain, and either no fever or a slight and temporary rise of temperature, and no other disturbance of the general health. The patient usually first notices trouble in the joint on getting out of bed, or during a walk, or on some other movement. The ligamentous attachments are tender, with some swelling of the peri-articular tissues, but usually there is no effusion into the joint and no redness of the overlying skin. Hydrarthrosis may occur, however, particularly in the knee, where it may distend the capsule and render movement difficult or impossible. Limitation to a single joint is exceptional, occurring in only about 8 per cent. of the cases. After a few hours or a few days other joints are implicated, but with less intensity, the last joint to recover being the one primarily attacked. All of the joints may be attacked successively, but usually the number is limited to three or four. In cases of hydrarthrosis the absorption is slow and may sometimes require immobilization of the limb. Restoration of the function of the joints involved, although sometimes requiring only a week, is usually protracted to a month or even several months, and is most obstinate when the smaller joints are affected. Lépecq(15), in his report of an epidemic of dysentery at Caen, states that some of his patients were made permanently helpless by the joint complications, and that some of his *confrères* had cases in which the arthropathies proved fatal.

The lesions are chiefly peri-articular, and rarely result in appreciable changes in the cartilages or ends of the bones, but occasionally, as in some of Vigne's(16) cases, there remain permanently some swelling and induration of the affected joints with impairment of motion. But once the cure is effected it is definitive. Recurrence of

the symptoms is unknown. Neither ill health preceding the dysentery, nor a severe course of the disease seems to predispose to these arthropathies. On the contrary, they are more frequent in robust subjects, who have been but little weakened by the dysentery, than in the weak and cachectic, and in the mild rather than in the severe cases. Exposure to cold or over-exertion was not observed as a possible causal factor.

Various theories have been entertained as to the nature of this complication, but no one of them is entirely satisfactory. Stoll(17), who regarded dysentery as simply an intestinal form of rheumatism, naturally found a ready explanation in a rheumatic metastasis to the joints. This rheumatic conception of dysentery dominated medical opinion for more than a century, and traces of it appear as recently as the last generation in Trousseau, who in his classification of the forms of dysentery describes a rheumatic variety with specially marked abdominal pains and articular metastases. The evidence is wholly opposed to this view. Dysenteric arthropathies differ from those of genuine rheumatism in the absence of fever or its slight and transient character when present, in the paleness of the skin over the affected joints, in the lack of a history of a preceding attack of rheumatism in all but a very small proportion of cases or of subsequent recurrence of the joint symptoms, in the absence of cardiac complications except in instances so rare as to admit of doubt in the diagnosis or of their reference to a true pyæmic affection, and in the fact that the joint symptoms of dysentery generally occur at a season of the year when rheumatic affections are exceptional.

Nor is the theory more tenable which bases these arthropathies upon a "morbid affinity" or a "reflex relation" between the articular and the intestinal lesions. "If the intestinal ulceration," as Dewevre well says, "be the starting-point of an articular reflex, why does so simple a mechanism so rarely come into play? why are not the most severe, the most ulcerative, the most irritating dysenteries, the most fecund in articular manifestations? and why are the latter so often delayed until the period of convalescence when the intestinal irritation is subsiding or has entirely disappeared?"

The explanation of the pseudo-rheumatism of dysentery by a mild pyæmia is equally open to objection. Pyæmic infection in its usual forms does occur exceptionally in dysentery as in other diseases

attended by suppuration, but with symptoms entirely different from those of the dysenteric arthropathies. In the latter the symptoms are habitually of a mild type, unattended by other indications of purulent infection, and generally occur when the intestinal suppuration is at its minimum or has been arrested by the process of cicatrization.

In their general character the arthropathies of dysentery are allied to the joint affections which occur in connection with a great variety of infectious diseases—scarlet fever, typhoid fever, smallpox, erysipelas, cerebro-spinal meningitis, etc. In all of these affections articular manifestations occur occasionally which are clearly not rheumatic or pyæmic, but appear to be due directly or indirectly to the primary disease. In the persistence of its symptoms this complication bears a certain analogy to gonorrhœal arthritis, but there the analogy ceases. Farther than this we cannot go at present without entering the region of pure conjecture.

Dysenteric Paralyses. Aside from passing allusions to the occurrence of paraplegia in dysentery by Galen(18) and other early writers, no important contributions to the study of the paralytic complications of this disease were made until the articles of Leroy D'Etiolles in 1856, and Gubler(19) in 1860. Since then cases have been reported and their pathology discussed by Delioux de Savignac(20), Leyden(21), Barié(22), S. Weir Mitchell(23), Woodward(24), Pugibet(25), and others. The reported cases are, however, so few and so incomplete in necessary details that it is difficult to come to a definite conclusion as to the pathology of a considerable proportion of them. Some were unquestionably accidental, having no causal relation to the dysentery.

Paralyses occur in both the acute and chronic forms of dysentery, sometimes during the course of the attack, but usually as a sequel. By far the most common form is paraplegia, but the upper extremities may be involved also, and hemiplegic and monoplegic cases have been reported, as well as paralyses of muscular groups in various parts of the body. Thus Pugibet describes two cases of complete bilateral paralysis of the extensor, flexor, and rotating muscles of the head with paralysis of the muscles raising the arms on the shoulders, and paresis of both upper extremities. In another of his cases there was paralysis of the left serratus magnus, with paresis of the left

trapezius and right rhomboideus. Diffused general paralysis has also been observed.

In some cases the onset is sudden, nocturnal, unattended by facial paralysis or mental disturbance, the paralysis developing rapidly (twenty-four to forty-eight hours) and lasting but a short time (three to twenty-eight days). In the affected muscular groups there are inequalities of loss of power, the paralysis is more complete toward the centre than at the periphery of the nerve distributions, and reës tablishment of function begins with the paretic muscles and ends with those whose motility has been completely abolished (Pugibet).

In other instances the paralysis has a more gradual development, and this appears to be the usual history of the paraplegic form. Paralysis of the vesical and anal sphincters, and girdle sensations are absent with very few exceptions. The paralysis is rarely complete in all the muscles of a limb or in muscular groups elsewhere. Among the muscles innervated by the same plexus or by the same nerve some may be paralyzed, others not. Sensory disturbances are usually not prominent, but in some of the reported cases, neuralgic pains, tingling sensations, cramps, and limited anæsthesias were observed. The conditions of the reflexes and the electrical reactions have not been studied with sufficient care to make the reports on these points of much diagnostic value.

In Pugibet's analysis of 17 cases, including besides his own, those reported by Moutard-Moretin, Barié, Delioux de Savignac, and Durozier, in 13 the paralysis lasted from one to one hundred and twenty days, and in 4 the paralysis was in a stationary condition at the time of the report. In two cases death occurred apparently as a result of the paralyzing lesions, and in four independently of them.

Woodward reports eight cases observed in the Northern armies during the Civil War, all of them paraplegias except one, in which the loss of power was confined to the left lower limb. In none was the paralysis complete. No autopsies were made. He calls attention to the similarity of the paralytic symptoms to those of lead poisoning affecting the lower extremities, and suggests that perhaps some of the cases may have been caused by the use of this drug in the treatment of the dysentery. In some remarks on this complication, Weir Mitchell says: "I myself have seen in the wards of the U. S. Army Hospital for Diseases of the Nervous System many

cases of palsy, chiefly paraplegia, following upon dysentery, acute or chronic; but in nearly every case there had been many possible causes, such as long marches, bad diet, malaria, or injuries to the spine—these being so common that almost any patient in long service had some to relate. It was thus difficult or even impossible to fix upon any single factor as most important or essential, when, as in the mass of cases, it was likely that several contributed to influence the final result." In some of his cases the symptoms yielded so promptly to tonics, good diet, and stimulants, that the paralysis appeared to be merely functional disturbances of exhausted nerve centres.

The pathological study of this complication has been very unsatisfactory. The opportunities for it have been comparatively rare, and of the reported autopsical examinations practically none have met the requirements of recent methods. The absence of gross lesions in the earlier examinations led D'Etiolles to the conclusion that dysenteric paralysis occurred without cord lesions, and the same view was adopted by Gubler, who classed them among the similar paraplegias that followed diphtheria, typhoid fever, cholera, and some other infectious diseases. Then came Brown-Séquard's(26) theory of "reflex paralysis," which had but a brief popularity, and was followed by Leyden's hypothesis that dysenteric paraplegia is due to an ascending neuritis starting in the intestinal wall and producing changes in the cord. Leyden's single case, upon the symptomatology of which he based this opinion, seems to have been one of what we should now regard as infectious multiple neuritis. The only autopsical examinations, to my knowledge, that have given positive results were two cases of Delioux de Savignac, in one of which there was softening of the cervical and lumbar enlargements, and in the other softening of the lumbar enlargement, the symptoms during life being a progressive paralysis, with final invasion of the respiratory muscles. In another case, reported by Damaschino and Roger(27), of a child two years of age with left hemiplegia and later paralysis of right leg, destructive lesions were found in the nerve cells of the anterior cornua such as belong to infantile paralysis.

Pugibet favors the central origin of these paralyses and expresses the opinion, which is, however, a purely theoretical one, that the cord changes begin with the occurrence of capillary thromboses and

limited ischæmias that may either be temporary or may lead to atrophy and softening of the nerve elements.

The whole subject needs further study. Of the reported cases some were clearly of central origin, organic or functional, but most of them appear to have been cases of infectious multiple neuritis—at least the absence of vesical and rectal paralyses, the incompleteness and irregular distribution of the loss of power, and the not infrequent association of sensory with motor disturbances, certainly point in this direction.

Treatment.

The treatment of dysentery hitherto has been almost wholly symptomatic and empirical, and must remain so until we have differentiated its several infectious causes, and discovered means for destroying them. In the meantime is it not possible that the contrariety of opinions as to the value of particular remedies is due, in part, to the fact that in dysentery we have to deal with a number of distinct affections, and that a drug valuable in one infectious form may be comparatively useless in others.

The Ipecac Treatment. The recent revival of the ipecac treatment for dysentery is quite as remarkable as its episode as a quack remedy in the seventeenth century. The treatment by large doses was introduced into India about thirty years ago by Mr. Scott Docker(28), surgeon to the second battalion of the Seventh Royal Fusiliers, and rapidly came into favor, superseding almost at once the old plan of blood-letting and mercurialization. It is often referred to, especially by German and French writers, as the emetic treatment, but this is a misconception of it, as the avoidance and control of emesis form an important part of the treatment. Twenty or thirty drops of laudanum or an equivalent dose of some other preparation of opium may be given for this purpose half an hour before the administration of the ipecac, but some authorities regard this as unnecessary and as interfering with the desired effects of the drug. A mustard poultice large enough to cover the entire surface of the abdomen is applied, and after its full action twenty to thirty grains of ipecac are given with only sufficient water to wash down the dose.

The patient must lie flat on his back, with the head low, keep absolutely quiet and refrain from talking for three hours, during

which time no food or liquid is to be given except some cracked ice or an occasional teaspoonful of water if the thirst be unbearable. Counter-irritation of the abdominal surface is to be kept up either by another mustard poultice, or, still better, by a sheet of spongiopiline wrung out of hot water. Under this management it is claimed that while there is always nausea, vomiting is generally avoided, or is delayed long enough to permit absorption of the drug. If vomiting occur early, the dose should be repeated after a suitable delay. Eight or ten hours later another, but smaller dose is given, and this double daily dose in gradually reduced quantities is repeated morning and evening for two or three days until the dysenteric symptoms have yielded or fail to respond to the treatment. The best results are obtained during the early days of the illness before ulcerative processes have begun, but even in chronic dysentery the acute exacerbations are said to be controlled by it, and as Prof. Maclean testifies from his own experience, most happy effects are sometimes obtained in apparently hopeless adynamic cases.

In 1868, a decade after the introduction of this treatment into India, the writer just mentioned says that "this system of treating acute dysentery is now almost invariably followed in India;" that it has reduced the former mortality by from 25 to 75 per cent. according to different reports, and that in his opinion it is "the most simple, the most successful, the most conservative, and the least distressing mode of treatment I have ever seen used in dysentery. Year by year under its use the number of chronic cases is becoming smaller, and hepatic abscess is less frequently seen." In 1883 Joseph Ewart(29), after a long experience with this treatment in India, speaks of it with the same enthusiasm, and says "that every physician who has used ipecac in heroic doses soon learns that depression of the vital powers is not to be feared, and is surprised at the small amount of vomiting that follows its administration." At the same time he admits the occasional occurrence of uncontrollable sickness and vomiting, but says it is seldom witnessed except in connection with such complications as abscess of the liver, malarial poisoning, splenic and liver affections, Addison's disease, Bright's disease, phthisis, peritonitis, or extensive intestinal sloughing—a list of possibilities that is anything but reassuring. Abundant testimony of an equally favorable character might be cited from other writers in

India, but of late years physicians in that country have become less enthusiastic about the advantages of large doses and more apprehensive of their depressing effects. Surgeon-Major S. T. Dobie(30) says that the treatment by large doses has fallen into disfavor. Chowdhovry(31) says that both in civil hospitals and in private practice it has been found unbearable in many cases, and that the constant sensation of nausea which worried the patients undergoing this treatment interfered greatly with their taking nourishment. Neither of these writers has lost faith in the ipecac treatment, but advocates its use in much smaller doses.

In England, where dysentery is now so uncommon that few physicians there have had much experience with it, the treatment has been but little used, though as recently as 1888 C. Hanfield Jones(32) speaks of it as "facile princeps medicamentorum" in dysentery. Dr. Clouston's results from it in the epidemic already mentioned were very unsatisfactory. He says that he used it in the earliest stages of the disease and in every possible way, by the mouth and by the rectum, in doses of from ten grains to a drachm; gave the drug alone or in combination with opium and after opium; administered it once a day or every two hours, and the result was a mortality of twenty out of thirty-one cases. In a few instances the drug caused vomiting that could not be stopped, and prostration that was never rallied from; sometimes it caused no sickness even in large doses, and then it diminished the quantity of blood in the evacuations, while in the majority of cases it produced temporary nausea without doing harm or good.

In this country the treatment has never secured a firm foothold. During the Civil War favorable results were reported by a few surgeons in the field, but trials of it, more especially in chronic cases at the Eckington Hospital, Washington, D. C., and later in Columbia, South Carolina, in 1868, were disappointing. Since then successful cases have been reported from time to time in medical journals, but the treatment has never met with general adoption, partly on account of the frequency with which depressing effects have been met with, and partly because the superiority of this over other less objectionable methods has not been demonstrated for the dysenteries of this country.

As to the great value of this treatment in certain cases there is no

doubt whatever. In such instances ipecac in heroic doses, given particularly in the initial stage, has seemed to act almost as a specific, promptly relieving the tormina and tenesmus, producing bilious feculent stools, and arresting the further progress of the disease. Such reports come to us chiefly from tropical and subtropical regions where dysentery is very frequently of amœbic origin, and possibly systematic examination of the stools in amœbic dysentery in connection with this treatment may show that ipecac has a special relation to this form of dysentery. Many recent writers who discard the large doses, recommend the drug in amounts sufficient only to excite slight nausea (two or three grains), or in still smaller doses, one-fourth of a grain every half-hour, as suggested by Loomis. My own preference has been for this method.

Opium. From the earliest use of opium in dysentery down to the present time there has been a long-standing controversy as to the therapeutic value of the drug in dysenteric affections. By one school of writers its use has been limited to the relief of pain, to moderating the frequency of the dejections, and to procuring sleep. By the opposing school opium, it is claimed, has not only these advantages, but also directly controls the inflammatory process. The history of this dispute is very interesting, but I can touch upon only a recent aspect of it. Probably nowhere else in the world is opium used with so much freedom in dysentery as in this country. This is due largely to the influence of the writings of Chapman(33), George Wood(34), Stillé(35), Flint(36), and Loomis(37), all of whom have been strong advocates of the view that in dysentery opium has marked antiphlogistic virtue. Flint leaves us in no uncertainty as to his own convictions. "In sporadic dysentery," he says, "after purgation opium in some form is the remedy to be most relied upon." Other remedies are suggested, but merely as adjuvants or to replace opium when from some idiosyncrasy it is not tolerated. In epidemic dysentery the great object, he holds, is to arrest the sero-sanguinolent dejections. Purgatives, especially of the saline class, may be used cautiously, but opium is to be the main reliance, associated with various astringents, but with these as merely auxiliary. The dosage of opium or morphine is to be measured by its effect in checking the discharges, care being taken, of course, that profound narcotism is not induced; but with this precaution, if the dejections be not controlled by small

doses, these may be increased "to the amount which will be borne without narcotism, be the amount never so large," even to twenty-four grains of morphine in the twenty-four hours, as in one of Flint's cases.

Loomis takes the same view as to the antiphlogistic value of opium in dysentery, and advises that it be given up to the point of semi-narcotism. Independently of its narcotic, sedative, and astringent effects, he maintains that it controls the inflammatory process by its action on the sympathetic nervous system.

On the other hand, to cite only a few recent authorities, Trousseau says: "When opium is indicated it is not for the purpose of stopping the intestinal flux, but for moderating the accompanying pains, and particularly for checking the vomiting which renders the administration of other medicines impossible." Heubner(38) opposes the methodical use of opium in dysentery and recommends it only as a temporary and palliative remedy. Joseph Ewart, after his long experience with the disease in India, says that opium is seldom required; that it checks the secretions of the liver, pancreas, and alimentary mucous membrane, favors rather than reduces the inflammation of the solitary and tubular glands, and masks the real character of the disease by inducing an apparent amendment of symptoms whilst destructive ulceration and sloughing of the mucous membrane is rapidly extending. Woodward, who had a better opportunity than anyone else in this country of estimating the value of the opium treatment of dysentery during the Civil War, says: "For myself, I freely confess that I went into the field at the beginning of the war in favor of the use of opium in all the alvine fluxes, which experience was very speedily modified. When I published my *Outlines of the Chief Camp Diseases*, in the latter part of 1863, I still favored its employment in a more liberal manner than I now approve, but already at that time I insisted that opiates should not be regarded as 'specific or curative agents,' either in acute dysentery or the chronic fluxes."

In the milder grades of dysentery it probably makes but little difference whether opium be used or not, except so far as the comfort of the patient is concerned. These cases recover, as Flint himself has shown, with a mere placebo treatment in about the same time as when subjected to various forms of active medication. The problem

is a very different one, however, when we have to deal with adynamic forms of infectious dysentery, in which, as in puerperal peritonitis, the profoundly depressed nervous system often manifests an extraordinary insusceptibility to the toxic action of opium. Flint's case has been already cited; to it may be added, as a recent illustration, Dr. Wright's patient who received twenty-four grains of opium by the mouth, thirty grains by suppository, and one and a half grains of morphine hypodermatically in one day without symptoms of narcotism or other unpleasant effects. Such a use of opium, it must be admitted, has the sanction of high authority, but there is no satisfactory evidence in its favor. What reason is there to suppose that in croupous and amœbic inflammations of the colon, opium has a direct influence in controlling inflammatory processes that we do not admit for it in typhoid infection of the small intestine or in diphtheria of the throat? The use of opium in dysentery as an antiphlogistic is not based on known properties of the drug, and the mere fact that patients survive even large doses does not counteract the strong objections to such an employment of it. It destroys the appetite, impairs digestion, favors the retention of decomposing and fermenting products, and can be justified only by a clear demonstration of its superiority over other less hazardous methods. Such proof we certainly do not possess.

In dysentery, as in other affections attended by excessive fluxes and severe pain, opium is of unquestionable value in moderating these symptoms, but it is most important to bear in mind that the cure of disease is not to be effected by mere suppression of its symptoms. Sixteen hundred years ago, Galen(39) warned the medical profession of his time that "those who resort to anodyne remedies at improper times or immoderately, jugulate the sick along with their pains." For my own part, experience has taught me more and more to distrust the fallacious effects of opium in dysenteric diseases, and I am quite sure that this conclusion is in accord with the opinion of most recent authorities.

Purgatives. The treatment by purgatives followed naturally upon the observation that acute colitis, at least in its early stage, is really a constipating affection, a "morbus alvum occludens," as Stoll called it, and that reappearance of fecal dejections is usually an indication of approaching resolution of the inflammation. In one form

or other this treatment has been in use from the earliest times and has unquestionable advantages. Besides removing scybala and other irritating material, it produces, when properly used, a sedative effect upon the inflamed intestine, as shown by the marked relief of tormina. Whether it also directly modifies the inflammatory process by a supposed alterative action or by depleting the intestinal blood-vessels, is questionable. Certainly the practice of daily purgation with this object in view is much less common now than formerly. Probably most, if not all, of the good effects from purgatives come from the cleansing of the intestinal canal. For this purpose it probably matters but little which of the milder purgatives is used. Some prefer the salines, sulphate of magnesia, sulphate of soda, Rochelle salt, or a seidlitz powder; others, castor oil. The latter is disagreeable to sensitive stomachs and has no special advantages. Purgation in acute cases every second or third day is all that is required. It is objectionable in adynamic cases, and unnecessary in the not infrequent cases with diarrhœal rather than dysenteric dejections.

Calomel. As regards calomel, which has played so important a part in the treatment of dysenteric affections during the first half of the present century, perhaps no better illustration of the general disfavor into which it has fallen of late years can be given than the absence of even any allusion to it by my friend, Dr. Osler, in his remarks on the treatment of dysentery in his work on the *Principles and Practice of Medicine*, published during the present year. Some of us remember vividly the order issued by Dr. W. A. Hammond, in 1863, then Surgeon-General of the Army of the United States, withdrawing calomel from the list of medicines supplied to the army, on the ground of the bad results following the indiscriminate use of this drug, particularly in the alvine fluxes, as well as the strong protests against this order made by many army surgeons and by the American Medical Association. The present reaction against the systematic use of calomel in dysentery, at least in this country, seems to be due partly to the unfortunate results from it during the Civil War, partly to the practical abandonment of it in India, and the better success there with other remedies, but chiefly, it seems to me, to the growing scepticism as to either the antiphlogistic or cholagogue properties formerly ascribed to this drug. How far this sceptical attitude is justified by recent destructive criticism on both of these points I am

not prepared to say. Probably the reaction has gone too far, and we are in danger of losing a valuable remedy in dysentery simply because bad results have followed the misuse of it. As an occasional purgative in sthenic cases, or used systematically in doses small enough to prevent depressing effects or risk of salivation, calomel is still highly recommended by some authorities. I have had no experience with this treatment. H. C. Wood(41) says that in his hands it has yielded better results in acute sthenic dysentery than any other remedy.

Corrosive Sublimate has been recommended highly by a few writers, particularly by Kopp(42) in 1827, Parkes(43) in 1846, and recently by Ringer(44). That this drug has a special relation to the colon, the glandular structures of which probably take the chief part in its excretion, is shown by the fact that after its absorption in poisonous quantities through other channels than the alimentary canal, as for instance by the skin, vagina, uterus, and wounded surfaces, the most conspicuous lesion is an ulcerative colitis closely resembling that of diphtheritic dysentery. Its mode of therapeutic action in this disease is unknown. When given in medicinal doses the amount excreted by the intestinal glands is probably too small for a germicide effect, and it is more reasonable to suppose that it acts either as a local alterative—a convenient term for concealing our ignorance—or by rendering the soil infertile for the growth of infectious organisms. As Ringer has pointed out, the best results are obtained in acute cases, especially those in which the stools are bloody and slimy. It should be given in small doses, $\frac{1}{120}$ to $\frac{1}{60}$ of a grain hourly, with or without one or two drops of laudanum.

Bismuth Subnitrate in large doses, as recommended by Monneret(45), is probably useless for arresting the morbid process in its early stage, but when the stools have become diarrhœal in character this remedy has a certain value from its sedative, astringent, and possibly its antiseptic effects. Monneret advised very large doses, from an ounce and a half to two ounces daily, but equally good effects are obtained with a much smaller dosage. With large doses one should be sure that the article is pure and free from adulteration with arsenic.

Salol. Within the past few years very favorable reports have been made of successful results with salol in acute dysentery. Dr.

W. P. Nicolson(46), Professor of Anatomy in the Southern Medical College at Atlanta, Georgia, says that he has had ample opportunity of testing this remedy, and that since he began using it he has found the resort to any form of opium unnecessary. Given in five-grain doses every hour in the early stage, he claims that it rapidly relieves the griping and tenesmus and restores the patient to a condition of comparative comfort.

Astringents. Nitrate of silver, the solution of pernitrate of iron, tannic and gallic acids, catechu, krameria, and hæmatoxylon are useless and may be even injurious in acute dysenteric affections, but are often valuable in their chronic forms.

The Local Treatment by topical applications to the rectum, or by flushing the entire canal below the ileo-cæcal valve, has grown rapidly in favor of late years. There are few difficulties attending either plan except during the early acute stage, but unfortunately this is just the period when local methods are most needed to arrest the local process and diminish the danger of constitutional infection. Trousseau says that the tenesmus of dysentery is not due to spasmodic contraction of the sphincter, and that he has often demonstrated to students that "the anus, in place of being tight and closed, is sufficiently open to allow the five fingers to be introduced," the tenesmus and acute burning sensation being due to the violent irritation and swollen condition of the mucous membrane rather than to a tight constriction of the sphincter. This is doubtless the case after some days of illness, when the sphincter muscle has been more or less paralyzed by the inflammation of the contiguous mucous membrane, but for the very outset of a dysenteric attack the statement is incorrect, as at this period there is often a constriction of the anal orifice and an exquisite tenderness that interferes seriously with the use of enemata, large or small. To relieve tenesmus or to prepare the way for effective enemata we may use suppositories of ice or suppositories containing four per cent. of iodoform as recommended by H. C. Wood(47), or a teacupful of warm water with twenty to forty drops of creasote retained for a few minutes—Tipton(48), or a starch and laudanum solution, or a cocaine suppository, or a small injection containing ten drops of a four per cent. solution of cocaine.

For thorough irrigation of the rectum and lower part of the colon the best apparatus is a double rubber tube or two catheters intro-

duced side by side—Dr. W. W. Johnston(49), but by this method the irrigation extends at most but a few inches beyond the end of the instrument, as the water escapes nearly as fast as it is injected. This may be all that is required for the cases in which the lesions are confined to this region, but as we can never be certain how far the morbid process extends, large enemata are to be preferred when they are practicable. The patient may lie either on his back or on his side, with his hips raised by a high pillow so as to favor the flow of the fluid into the intestine by gravitation. A large soft catheter or a small rubber œsophageal tube connected by tubing with a funnel, and with a small roller bandage wound around the terminal tube eight or ten inches from its distal end, to serve as a plug for preventing the escape of the enema, is introduced well oiled into the rectum until arrested by the bandage, which is to be pressed firmly against the anus. The funnel is then raised not more than two or three feet so as to allow the fluid to flow in very gradually with a low hydrostatic pressure, and the connecting tube is compressed from time to time to permit the intestine to adapt itself to the distending process.

To irrigate the entire colon from three to four pints are necessary. Unless the bowel be very sensitive, this amount can usually be given without much difficulty by the gradual method. Large enemata are tolerated best soon after a movement of the bowels. The first one should be given by the physician himself or a competent assistant; later ones may be intrusted to a nurse who can be relied upon to follow the method strictly. Irrigations may be carried out either with pure water or with medicated solutions. If water alone be used, it may be given either very hot or very cold. In acute sthenic cases ice-water injections have proved very effective, but in adynamic or chronic conditions hot water is preferable. In either form large enemata of simple water have a very happy effect in many cases, quieting the tormina and tenesmus and diminishing the frequency of the dejections. In fact, the favorable reports with medicated solutions have been due in large measure to the sedative action of the heat or cold, and to the mere removal of irritating material from the surface of the mucous membrane.

With medicated solutions the best results have been obtained with corrosive sublimate, nitrate of silver, quinine, alum, and creolin.

Lemoine(50) reports marked success with mercuric bichloride solutions, 1 to 5000 and 1 to 3000, thrice or twice daily, in fifty-four cases, both acute and chronic, at the Military Hospital at Oran, Algeria. In the acute cases the enema was preceded by the application to the anus of a pad saturated with a strong solution of cocaine. The injections invariably relieved the tenesmus, the mucous stools disappeared after three or four days, and no case was followed by stomatitis or other evidence of mercurial poisoning. Careful examination of the urine in five cases failed to show the presence of mercury, and from this observation Lemoine concludes that the drug is not absorbed in dysenteric inflammations, whatever may be true of physiological conditions of the colon. In the strength of the solution, and in the small quantity (six ounces) employed by Lemoine, bichloride enemata may be entirely safe, but it by no means follows that they are free from danger in amounts necessary to flush the entire colon, as this would necessitate the use of from eight to ten grains of the drug. In view of the occasional occurrence of sublimate colitis from irrigation of mucous surfaces with bichloride solutions, the safer plan would be to first flush the colon with water and then give a half-pint mercuric enema.

In *amœbic dysentery* solutions of quinine, 1 to 5000, 1 to 2500, and 1 to 1000, have been used by Councilman and Lafleur in five cases. The treatment was suggested by Lösch's(51) observation that outside of the body the amœbæ were killed by a quinine solution of 1 to 5000. In three of the cases "the amœbæ disappeared from the stools after a more or less prolonged use of the injections," but returned in small numbers when they were discontinued. In the fourth case, fatal from hepatic abscess, the injections were stopped on account of the patient's hopeless condition, and in the fifth, which was still under observation, "the amœbæ were quite as numerous as when the treatment was first instituted." A pint or a quart of the quinine solution was injected thrice daily with the patient in the knee-and-elbow position, the enema being retained for fifteen minutes and followed by friction along the course of the colon. These injections, the writers claim, do destroy the amœbæ in the contents of the bowel, but whether they do so in the tissues they admit is an open question, and suggest a further trial, particularly in incipient stages of the disease.

My own experience with this treatment is limited to the following case, which is particularly interesting as showing that while amœbic dysentery is commonly a tropical affection, it may originate even as far north as Winnepeg, Canada:

The patient, a Scotchman, who had lived in that city for two years, was attacked last August with diarrhœa, which, after two or three weeks, was followed by dysenteric symptoms—mucus, bloody discharges, tenesmus, and tormina. He was confined to bed for a month with this acute attack, and then for the next four months diarrhœa was followed by constipation in alternating periods of two or three weeks' duration. In April, after a month's freedom from diarrhœa, he left Winnepeg to take a steamer at New York for Glasgow, Scotland. On the way he had a relapse, and when admitted to the New York Hospital on April 27th, was having from three to six stools daily, containing fecal matter, mucus, no blood, and a large number of amœbæ. He was put upon a milk and meat diet, with salol in five-grain doses thrice daily, and two quarts of a quinine solution 1 to 3000, later 1 to 5000, were injected morning and evening. Under this treatment the stools, which were examined almost daily by Dr. Frank Ferguson, the pathologist of the hospital, did not diminish in frequency, but the amœbæ gradually disappeared, first the live ones, and then even the dead ones. On May 5th salol was changed for bismuth subnitrate, and from this time the diarrhœa rapidly ceased. For the past ten days there have been no stools except after the enemata, no more amœbæ have been found, and the patient is regaining his strength, but the case is too incomplete to permit any conclusion as to the final result.

In *chronic dysentery* no topical application has proved so efficient in my hands as large enemata of nitrate of silver, one or two grains to the ounce. In this strength they rarely cause much pain. The first effect is sometimes to increase the frequency of the dejections, but this temporary aggravation lasts only one day. Occasionally a very striking improvement is observed from a single enema, but usually the treatment has to be repeated once or twice daily for several days. When not continued longer than this there is practically no danger of argyria, and no necessity for following the silver enema by one of a common salt solution, as recommended by some writers. In acute dysentery it is best to begin with very weak solutions, $\frac{1}{16}$ or $\frac{1}{8}$ of a grain to the ounce, and then rapidly increase the strength as the bowel becomes tolerant of the drug.

Good results are reported also with enemata of alum twenty grains to the ounce, cupric sulphate two to five grains, creolin four grains,

iodoform two to six grains suspended in starch mucilage, salol one grain, and with an eight per cent. solution of peroxide of hydrogen.

As regards the question of danger from large enemata in dysentery, anyone who has seen a colon riddled with ulcers, some of them perforating to the peritoneal surface and just on the point of rupture, must admit the possibility of a fatal accident from sudden and forcible distention of the gut. I am not aware, however, that rupture has ever been produced in this way in dysentery, and Dr. Osler is mistaken in quoting me as having reported the case of a child in whom general peritonitis followed such an injection. The only instance that I can recall in which death was caused by a rectal enema was that of an old man with rectal cancer, and probably cancerous or decubitus ulceration above the point of stricture. To relieve an acute attack of constipation his homœopathic physician administered an enema which was rapidly followed by collapse and symptoms of perforative peritonitis. No autopsy was made, but there was no reasonable doubt as to the cause of death. The chances of such an accident in dysentery may be very small, but the mere possibility of it when ulcerative processes are suspected should make us careful to introduce enemata with the lowest necessary hydrostatic pressure.

The present popularity of local methods of treatment for dysenteric affections is not, I believe, merely temporary. So far as they are practicable they are as much indicated in colitis as in inflammations of other accessible mucous membranes, but too much must not be expected from them. In some acute cases they cannot be carried out effectively, while in chronic dysentery the local pathological conditions are often beyond remedy, to say nothing of the hepatic and other remote changes that cannot be reached in this way. But even with these drawbacks the plan is rational, and when carried out properly as to method and cautiously as to the drugs used, is a most valuable addition to our therapeutic resources in dysenteric diseases.

Dietetic Treatment. As the limits assigned to this paper have been already exceeded, I can touch only very briefly on two points in the *dietetic* treatment. From ancient times there has been a very common prejudice, both in our profession and among the laity, against the use of milk in intestinal fluxes, and clinical experience has shown that it is not without some foundation. Although no

article of food agrees so generally with these patients as milk, when given perfectly fresh, or peptonized, or diluted with lime-water, or in the form of whey, koumiss, or matzoon, or in frequently repeated, small rather than large portions, this diet needs careful watching. Not only may digestion be overtaxed by mere excess in quantity, but one has to bear in mind also a possible idiosyncrasy on the part of the patient, adult or infant, that makes milk intolerable in any amount or in any form. Such cases, I admit, are rare. Usually the fault is with the form of milk or its method of administration, but this more or less complete intolerance does occur in intestinal fluxes and is often overlooked. The stools should be examined habitually for undigested curds, and when these are present the milk must be reduced in quantity, or given in another form, or abandoned entirely, at least for a time.

The other point is the importance of a liberal use of meat in chronic forms of dysentery. Graves(52), in his clinical lectures, says: "I have found several cases which had obstinately resisted the most varied remedies assiduously employed, get well rapidly after a liberal allowance of meat was given; and at present, when called on to treat a case of dysentery of long standing, the first thing I do is to put my patient on full meat diet." I have found this suggestion of much value in my own experience. These patients are always anæmic and full nutrition is essential. In no way can this indication be met so well as by meat in any easily assimilable form, such as scraped-meat, raw or partly cooked, salted and peppered to the taste of the patient, or, when bread can be digested in small quantities, scraped meat sandwiches, with the thinnest possible layers of bread, or even tender cooked meats in the usual forms when the patient can be relied upon to masticate them perfectly.

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ON THE TREATMENT OF ACUTE DYSENTERY BY ANTISEPTIC RECTAL AND COLON IRRIGATION.

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THE history of the rectal treatment of dysentery is a very interesting one, but I must resist the temptation to enter upon it. It dates back to the Egyptians, Greeks, and Romans, and had alternations of a century of favor followed by centuries of disfavor and abuse. The ancients employed it for the removal of "acrid humors," which they thought by their retention intensified the inflammation, and to this same idea have we come again with the help of fifty years of microscopic and chemical study. Coming down to recent years, there is one period in the history of this treatment to which I must refer.

IRRIGATION WITH COLD AND WARM WATER.—It is a matter of some interest to us that a physician of the neighboring and historic town of Bladensburg was the first to recommend cold water injection in dysentery. In the *Edinburgh Journal of Medicine*, in 1826, Dr. Joseph Kent, of Bladensburg, wrote that since 1823 he had employed ice-water injections for dysentery at half-hour intervals, "speedily alleviating every distressing symptom." In 1848 Assistant-surgeon Whitecomb, in a Calcutta medical journal,[1] reported two cases successfully treated by high injections with a long tube. But it is to the published opinions of Drs. O'Beirne and Hare that special attention should be paid. O'Beirne, in an article on "New Views of the Process of Defecation" (Am. ed., Washington, 1834, p. 35), held that in dysentery "the chief curative indication should be to

[1] India Reg. Med. Sci., Calcutta, 1848.

pass up the gum elastic tube and introduce it into the sigmoid flexure, in order to give exit to the accumulated and pent-up contents of the cecum and colon." In an appendix he writes: "Dysentery having appeared in this city (Washington) I have had opportunities of trying my novel mode of treating the disease." One to four pints of warm water with castor or olive oil were thrown in; hardened feces, mucus, and flatus were passed with relief of the symptoms.

Hare[1] used these words, full of meaning to us now:

"The substance of the whole argument is this: the long tube changes a huge internal abscess into an external one, and enables us to wash out and cleanse from it its putrid contents. It also enables us to foment and soothe by local applications the sloughing and ulceration these contents have caused on its surface. . . . Dysentery in its primary nature . . . is a mild and harmless disease, and . . . therefore if we remove quickly these acrid secretions we shall disarm dysentery of its terrors."

He advises the physician not to cease repeating the injection until he is satisfied that the colon is evacuated and cleansed; it is as necessary to wash out the colon when its contents are liquid as when they are solid.

"By passing an elastic tube beyond the sigmoid," he says, "I have found in more than three hundred cases of the severest form of dysentery not the slightest difficulty in washing out the colon from cecum to anus. . . . In treating three hundred and forty-six cases in Calcutta, I had but $4\frac{3}{4}$ per cent. of deaths.

It is a matter of some little pride to us that two of the three or four who first demonstrated the value of this mode of treatment should have been so near to us, the one our near neighbor, employing iced-water injections, and the other a surgeon of the army residing in Washington, advocating and using irrigations with large quantities of warm water thrown into the sigmoid flexure, with a view of cleansing and washing out the bowel.[2]

Antiseptic Irrigation.—As far back as 1774 we have records of efforts to modify the putrescence and gangrenous destruction of

[1] Edinb. Medical and Surgical Journal, 1849, vol. lxxxii., p. 40.

[2] Cold-water injections or irrigation have also been advised by Baker (1825), Dulles (1877), Messemer (1878), Dagand (1879), Laporte (1879), and Simon (1886).

Warm or hot water has been advised and used by Irving (1849), King (1872), Reid (1876), Kingsley (1887), Graham (1887), and Fordyce (1886). By some of these writers water irrigation was used as a preliminary step to the injection of drugs in solution.

tissue by antiseptic injections.[1] Peruvian bark, chamomile flowers, calumba, charcoal, chloride of lime, hypo-sulphite of soda, creasote, and other substances have been employed for the purpose by various physicians from that date until the introduction of the more successful antiseptics of the present day. In 1879, Cantani,[2] after treating of rectal alimentation, speaks of disinfecting the colon in dysentery and other diseases by such drugs as carbolic acid, salicylate of soda, borate of soda, etc., and predicts a great future for this kind of treatment.

Two causes have coöperated to draw renewed attention to rectal and colon antisepsis; one is the growing belief in the specific and contagious nature, with the recent discovery of the amœba of dysentery; the other is the dissatisfaction with other methods and the effort to find in this disease a direct, rational, and successful treatment.

I will not refer to all that has been written on this subject, but for three or four years past the journals have contained some favorable reports of this method. It will be noted, however, that few of them refer to *irrigation;* injection is the usual plan.

The latest communication is one that I have had translated since this paper was written. It is by Dr. Korytin,[3] a Russian. He refers to Dr. Strhogloo,[4] as having published, five years before, the results of his treatment of washing out the bowel with a 5 per cent. solution of carbolic acid. Sixteen cases are reported with excellent results. Dr. Kamper in the same year reported the same method used in eighteen cases. Korytin employed warm water or warm carbolized water. One tube only was used, and the fluid (six pounds) was allowed to remain in the intestine five to ten minutes, even fifteen to twenty minutes. One to three washings were generally sufficient; sometimes four to six were given, never more than one daily. Nine of the cases were severe (diphtheritic); six were milder (catarrhal). The improvements noted after the injections were: the number of the stools diminished; the frequent desire lessened; appetite, sleep, and the nervous state were all improved. The feces became thicker, lost their foul smell, and the mucus, blood, and particles of waste

[1] Pringle: Obs. on the Diseases of the Army, 7th ed., London, 1774, p. 275.
[2] Presse Méd. Belge, Brux., 1879, xxxi. 275.
[3] Vrach, 1890, xi. 957.
[4] Russkaia Meditsina, 1884.

tissue disappeared; the fever subsided. In the mild forms the results were happiest. In them tepid water had as good an effect as the carbolized warm water. The history of each case is given in detail, showing that the improvement followed immediately upon the washing of the rectum, and that relapses due to its suspension were arrested at once by a return to the treatment. In one fatal case after irrigation the stools were reduced from twenty to five daily; tormina and tenesmus lessened, but the patient grew weaker and died; gangrenous lesions in the bowel were found. In many of the cases internal medication was tried, proved ineffectual, and recourse was then had to the washing. The duration of the case after beginning the treatment was three, and in the most severe cases seven, days.

The strong arguments for the superior advantages of antiseptic irrigation are found in the complete and successful manner in which it answers to the pathological conditions of dysentery. An intense inflammation, seated in the rectum, sigmoid flexure, and colon, and always more intense here, even when the disease extends higher up, characterized by gangrenous destruction of tissues and ulceration with decomposition, and accompanied and most probably due to bacterial multiplication. If these conditions existed *outside* the body there would be but one course followed; the removal of the cause, if possible, then cleanliness and thorough antisepsis. Within the intestinal canal the typical treatment would be the removal of the cause or contributing cause, and cleanliness by thorough flushing of the bowel and antisepsis. There can be, there *must* be, but this one principle of treatment, and if the mechanical difficulties involved are removable, it must be the *successful* treatment.

There is one feature in dysentery to which I wish to draw separate attention—it is this: The rectum and colon form a distensible cavity and are closed below by the sphincter. In dysentery this cavity, especially its saccular and most dilated lower portion, becomes the most distended, the most filled by the contents, which are composed of transuded serum, blood, decomposing shreds of tissue, and the results of digestion, the whole being in an active state of disintegration and filled with multiplying bacteria. The sphincter, as a result of neighboring inflammation and œdema, acquires great irritability, dilates frequently, but with irregular and spasmodic movement, and contracts quickly and violently, closing the orifice before the rectum

is completely emptied. Thus the rectum becomes like an acutely inflamed bladder. A certain quantity of its contents is expelled; a residuum is always left; in some cases the amount is small, in others —bad cases with much fluid—it is large. The rectum is never emptied, but always contains some fluid in state of active decomposition. In this condition, as in a distended bladder full of decomposing urine, the first indication is to empty the rectum, and the second to wash out the cavity and to keep it empty and clean.

If this statement which I make is true, it has a most important bearing on the nature of dysenteric symptoms and on the kind of treatment which they require. I have found no reference to the fact in any work on medicine or in any medical contribution on the subject, although in the enormous mass of literature on dysentery the failure to find such a reference might well be excused. That it is a fact, I have demonstrated in several cases to my own complete satisfaction, and, although it may not be an essential feature in all cases, yet in a large number, and those the most severe, it is a constant condition.

The patient whom we see straining at intervals of a few minutes in his violent efforts to empty the rectum, does not empty it, the very intensity of the muscular contraction defeating this object. The sphincter shares in the irritability of all the rectal muscles, and closing spasmodically shuts off the escape of the contents before the act is accomplished. The result is also in part brought about by the patient lying down while straining, and the more feeble from prolonged illness he is the more likely is the rectum to be incompletely voided. Moreover, the routine treatment in dysentery helps to aggravate this retention; opium suppositories paralyze expulsive muscles but do not relax the sphincter; the number of actions is lessened and they are smaller, but the dangers are increased in proportion to the apparent success of the treatment, and the more severe the case and the more energetic the treatment the greater is the danger. In graver forms we have the more abundant, dirty white purulent and fetid stools, and the reddish-brown fluid with floating shreds of diphtheritic dysentery. The abundance of fluid favors its retention and accumulation, and every opportunity is given for the absorption of poisonous materials and systemic infection. Under such circumstances can any course seem more unreasonable than the ordinary

treatment adopted, and can any course be reasonable except one which applies general and accepted principles to the peculiar physical conditions of dysentery. *Keep the colon and rectum empty and clean;* that is the law and the whole gospel.

The following are two illustrative cases:

Case I.—Miss S. was taken ill on the night of May 28th, with an attack of severe abdominal pain and so-called diarrhœa. Paregoric was given at intervals then, and on the 29th, 30th, and 31st, the actions becoming more frequent, smaller, and showing blood. I was sent for in the night of the 31st. She was suffering from intense pain, and was much exhausted by frequent rising to stool; I gave a hypodermatic injection of morphia and stimulants internally, and suppositories of morphia were ordered.

June 1. Some nausea and vomiting. Two actions, reddish in color, and offensive, of thickish fluid, about two ounces each time. Stimulants, liquid food, and poultices to the abdomen ordered, and a saline purge as soon as she could take it. By the afternoon she had taken two purgative doses, and had had four stools, the last more fecal in appearance with a small scybala, but containing some blood.

2d. Had a moderately good night; two suppositories used. Three small stools, brownish fluid containing some blood. Champagne, milk, and whiskey during the night. During the day she had three stools of reddish-brown fluid with tenesmus; pain in the rectum and abdomen. At night she was worse and more nauseated. The actions were more frequent, consisting of a small amount of fluid, like uncooked beef tea, passed with tenesmus and causing vomiting.

3d. The stools occurred every hour, and were of the same character, fluid, offensive, and reddish. The desire to empty the rectum and the burning pain in the anus were constant. She had every indication of being weaker and more ill than before. A soft-rubber tube was passed into the rectum and about two ounces of fluid of the same character as had been passed before, flowed out through the tube. A smaller soft-rubber tube was passed by the side of the escape tube, and the rectum was irrigated with a continued stream of warm water with dissolved boric acid, until the water ran perfectly clear. A suppository of a quarter of a grain of morphine was then introduced.

During the day from this time on there was no action. At 3 P.M. the tube was again passed, and about one ounce and a half of fluid of the same character escaped. Irrigation as before, and suppository introduced. At 10.30 P.M. there had been no stool and the patient was much stronger in pulse and manner; had had no nausea, and had taken a good deal of nourishment, chicken broth and milk and brandy. Tube then introduced and escape of fluid as before; irrigation and suppository. During the night she was comfortable, and there was no action until 7 A.M. Two suppositories were used.

4th. There were two irrigations practised during the day with the same result as yesterday. The rectum was first emptied of a small amount of fluid,

more brownish than before, then washed out, and a suppository introduced. There was nothing else passed from the rectum all day. The night was comfortable.

5th. A dose of oil was given as there had been no action; this produced six actions during the day, four contained some solid matter and the last two were thin and brownish; there was no blood. No irrigation to day in consequence of the frequent actions.

6th, and for three days after, the rectum was washed once daily; there was no pain or diarrhœa, and her general condition continued to improve daily.

The two points in this case I would draw attention to are:

First. The fact that the rectum was not emptied voluntarily, although the stools were frequent on June 2d and 3d; and, *second*, that the complete evacuation of the rectum and the antiseptic irrigation at once relieved the distressing symptoms, both local and reflex; thenceforth the patient had no escape of fluid from the rectum except through the tube—that is, no action of her own assent or volition; the morphia, of course, contributed to relieve the irritability of the rectum and sphincter.

Case II.—Mrs. Y., an elderly woman, of about sixty five years of age, who had had a dysenteric attack in 1889, was taken with symptoms of extensive colitis in July, 1890. The chief symptoms were fever; feeble pulse; coated, dry tongue; no abdominal pain; frequent fluid evacuations, two to four ounces each time, of a dark-brown, very offensive fluid, containing small masses and shreds of mucus and a very little blood. She tried to resist the frequent desire, but every half hour to hour the anus would open and discharge and then spasmodically close with pain and burning. I tried for three days to relieve her by giving opiate suppositories combined with liquid food. But she made no change for the better, and finally I succeeded in inducing her to let me try a thorough washing of the rectum. I brought her to the edge of the bed in the position for a dorsal uterine examination, and introduced a small bivalve vaginal speculum into the rectum. This was done gradually, without causing much pain. Several ounces of the same ill smelling fluid escaped from the rectum when the sphincter was relaxed. The rectum was then thoroughly washed out with a five per cent. solution of carbolic acid. All other treatment was suspended. There was an immediate relief to the tenesmus and to the constant and uncomfortable desire to evacuate the rectum. The bowels were not moved until the following day, the discharge being of the same character but less in quantity and less offensive. From this time the rectum was cleansed twice daily for four days; the voluntary stools ceased, the fluid washed out contained mucus shreds, and, without a purgative, normal fecal matter was passed after the third days' irrigation.

In this case the situation was continued rectal and colon inflammation with beginning ulceration and retention of the decomposing fluid

in a distended rectum, consequently increasing danger of infection. The treatment was followed by immediate good.

I will add no words of argument to these facts, which so clearly show the uselessness, the waste of time in mouth treatment by drugs, and the rational application of a simple and obvious principle to the relief of a local disease.

Methods of Irrigation and Antisepsis of the Colon and Rectum.—In the earlier methods of rectal and colon treatment water was thrown into the bowel, retained for a certain time and then expelled. Some of the most excellent results are reported from this plan and within recent date. But this cannot be but an imperfect way of cleansing the bowel, although it answers well enough for bringing an antiseptic fluid in contact with the wall of the bowel and with germ-breeding mucus. The objections to it are, the necessity of distending the inflamed coats of the bowel up to a point where injury may be done, if any considerable quantity of water is injected; its advantages are that by this distention the antiseptic fluid washes the inner wall more thoroughly than without it. The method is better fitted, therefore, for subacute cases or those tending to become chronic, than for the acute inflammation with necrosis of the mucous coat. Properly speaking, this method is not irrigation at all, and the only procedure deserving of this title is that in which there is a *free* and *immediate escape* of the water thrown in; and even without argument, it is apparent, that in this way only can the bowel be thoroughly emptied and made aseptic.

The mechanical difficulties are very much greater in the efforts to irrigate the colon than in the case of the rectum. To wash the *rectum*, a double, in-and-out, hard-rubber tube, passed into the rectum five to eight inches, through which flows a current of water from a fountain syringe, answers the purpose well. The only objection is the pain which attends the introduction of a hard, inflexible instrument through the irritable anus. Two soft-rubber tubes passed side by side, the larger one for the escape current, are more comfortable for the patient and better in every way; number 17 English (29 French) is a good size for the smaller tube, the escape tube can be two sizes larger. A large-sized soft catheter will do very well for the entering current. The double-current soft-rubber tubes are not so successful; their soft and thin walls are pressed upon by the

sphincter and escape of fluid is obstructed. Then, again, there is an advantage in having two separate tubes, as either can be pushed up or down as it is desired to wash different parts of the rectal wall; they are, therefore, to be preferred to any double-current tube. The disagreeable sensation of distending the anus passes away in a few moments, and the patient gets so much relief from the operation that he ceases to object to it; preliminary cocaine applications may be used if the suffering is great.

All that is needed, then, for this operation are a fountain or Davidson syringe, attached to a small rubber tube or large silk catheter, an escape tube of large size of soft rubber, made long enough by the attachment of a long piece of tubing, so that the fluid escapes into a vessel on the floor. The hand holds and guides the tubes and changes their position from time to time.

The *colon* cannot be distended with water or irrigated with the same facility. That water can be made to pass through the sigmoid flexure there can be no doubt; but the passage of a tube through the flexure into the colon is a difficult task. If this is tried on the cadaver with the abdominal wall removed, one can see how difficult it is; the end of the instrument must describe a complete sharp curve on itself, as if it were about to tie itself into a knot. Even with the hand pressing on the passing instrument and guiding it, it is not easy to accomplish. It is clear from the experiments which I have made that a partially flexible tube, like the old-fashioned stomach tube, should never be used, and that a small tube does not pass as readily as one which more nearly fills the bowel. Distending the rectum with water as the tube advances does not favor the passage as much as leaving the bowel empty. The tube finds its way better along the mucus covered mucous coat. I speak now only of experiments on the cadaver, when the eye is watching the process; the contrary is the general opinion of physicians from efforts on the living patient. But the turning of the instrument on itself in a cavity filled with water, when the end strikes against the wall, is very likely to happen, and can easily be mistaken for the onward progress of the instrument. In the rectum the finger introduced discovers the error of direction, but higher up it is not possible to do so.

The conclusion of many trials must convince any one that the attempt to make the instrument enter the descending colon as often

fails as succeeds. The difficulties show that all colon irrigation must be done by one tube. I have tried the double current stomach irrigator, and have had constant failure; the closure of the lumen from twists of the tube or from outside pressure, prevent the exit of the injected fluid; so that the only way in which this can be accomplished is to force half a pint or one pint of fluid into the colon and then allow it to escape at once through the same tube; in this way the colon and sigmoid can be thoroughly washed out.

What are the indications for the choice of colon or rectal irrigation? In all cases of so-called catarrhal dysentery where the stools are small and contain blood and mucus, and in all cases, mild or severe, where the general or local symptoms are relieved by washing the rectum no attempt need be made to do more than this. For even when the disease extends into the sigmoid flexure and colon, the curative influence is transmitted along the bowel wall upward, as gargling the throat benefits laryngeal inflammation. If the patient continues to have fever, delirium, great restlessness, or other symptoms of general infection, or if the stools are large and thin, with a gangrenous odor, and contain blood, mucus, and tissue-like shreds, then the attempt should be made to pass the tube in the sigmoid for higher injection. If the patient is on his left side, with his hips raised, a gentle current may be passed from a raised fountain syringe into the colon, even if the point of the tube has not passed beyond the first curve of the "flexure." I need not add that there is a danger of perforating an ulcer, even without much force being used, so that the operation should be done with the greatest gentleness. In the great majority of cases of dysentery as we see it, rectal irrigation may, I hope, by continuing experience be proved to be all that we need to gain the desired end.

The *quantity* of water used depends upon the circumstances of each case; as a rule, it should pass in and out of the bowel until it runs clear, and both in the case of the colon and rectum the amount thrown in should be equalled or almost equalled by the amount which escapes; if the egress is not free the operation must he stopped until the trouble is remedied. There need be no limit to the quantity of water.

The *frequency* of irrigation is to be regulated by the number of stools, state of decomposition in the bowel, and other conditions; a good

rule *is to try to prevent the patient from having any stools at all;* let his bowel be emptied only *at your command* through the inserted tube; at first once in three hours, later three times daily, as the outflowing fluid contains less blood and has less odor. *Keep the rectum empty and clean,* is the one rule. At first wash the bowel once in three hours; later three times daily, and so on with diminishing frequency as there are less odor, less blood, and finally less mucus. When mucus is no longer seen in the form of thin flakes the patient may be said to be well; but for a few days one daily irrigation serves a good purpose. Relapses should at once be met by a return to local treatment.

As an *irrigating fluid* water may be used plain, hot, or cold, or may contain in solution any of the numerous antiseptics. Extreme cold or very hot water may be injected, but both must have a more or less irritating effect, and their action, in the nature of things, is intermittent. If a continued current of cold or hot water could be kept on the inflamed surface the case would be different. The surgeon would not apply great heat or cold for five minutes to an inflamed ulcer of the skin, and then leave the ulcer alone for three or more hours. It may be practicable to keep water flowing in and out of the rectum for many hours, but few patients could bear such continued distention of the sphincter.

Almost every *antiseptic* has received warm recommendation. Fifty-three cases of acute dysentery were treated at the Military Hospital at Oran with a 1 : 5000 bichloride solution. After the first day the stools were fewer in number, and in three or four days the mucus disappeared; tenesmus and pain were soon lessened.[1] Lemoine[2] treated fifty-four cases of dysentery with solutions of corrosive sublimate, 1 : 5000. Six ounces were injected into the rectum twice daily; later a solution of the strength of 1 : 3000 was injected twice daily. The fluid was not retained longer than ten minutes. Improvement followed immediately, and acute cases were cured in from one to three days. No systematic poisoning followed in any case. Notwithstanding all this favorable testimony, the dangers of ulceration in the colon being set up by the remedy, and the grave doubts lately raised as to the value of corrosive sublimate as a germicide in

[1] Centralblatt f. klinische Medicin, No. 11, 1891.

[2] Bull. Gén. de Thérapeutique, Paris, 1890.

just such conditions as exist in dysentery, deter one from using it at all. Under no circumstances should it be employed without an immediate outlet for the solution.

Tannin destroys bacterial life and renders ptomaines innocuous; it is recommened by Cantani for typhoid fever, but it may have as good an effect in dysentery for the same reason.

Salicylic acid, thymol, aseptol, sulpho-carbolate of zinc, alum, hydrochloric acid, carbolic acid, boracic acid, and the sulphites and hyposulphites have all been used and advised, but no sufficient number of cases have been treated by any one of these as to lead to its preference over all other remedies of the same class.

Boracic acid and carbolic acid are the only antiseptics I have used frequently; the results have led me to think that the former, or both together, give all we want, and as I believe that a great part of the benefit comes from the cleansing and complete emptying of the rectum, the least irritating and least dangerous germicide ought to be preferred.

A CONTRIBUTION TO THE STUDY OF HEPATIC ABSCESS.

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This paper was suggested by several cases occurring in my own practice, or seen in consultation, in which some of the most characteristic of the usual symptoms or signs of hepatic abscess were wanting when such an abscess was present, or else in which the symptoms were singularly suggestive of the affection and yet no abscess existed. It is based in great part upon the analysis of one hundred and eight cases collected from various sources, but I have in some places, when it seemed advisable, utilized other materials as well as this. The paper is not intended as an exhaustive review of the subject, but I trust the facts which I hope to bring out will help to clear up some of the obscure points in connection with this disease.

The first question which presents itself, of course, in any systematic study of suppuration in the liver is the nature of the germs or substances which cause this suppuration, but I do not feel qualified to express an opinion on this point. It seems to me, however—if I may venture to express *any* opinion—that the investigations of Hankin, of Prudden, Hodenpyl, Welch, and others tend to show that there are quite a number of germs and substances which are capable of causing pus formation under favorable conditions. That some bacteria or their products, however, are directly connected with the formation of hepatic abscess is almost if not quite certain, and we have next to inquire *from what points these bacteria or their products come and through what channels they reach the liver.*

There are several conceivable channels through which pyogenic germs or substances may reach this organ.

By the bloodvessels. Entrance of germs by the hepatic artery was

formerly considered a common cause of hepatic abscess, and it was claimed that injuries of the head, or of the bones generally, were especially apt to cause this affection. Frerichs, for instance, stated that "the supervention of hepatic abscess from inflammation of the veins of the systemic circulation was of far more common occurrence than abscess arising from phlebitis of the portal veins;" but this view does not accord with the facts, so far as definite information can be obtained. Waldeyer found hepatic abscess in only six per cent. of those who died from surgical diseases, while embolic processes in the lungs were present in more than two-thirds; and Klebs found that "thirty-two cases with metastasis in the lungs occurred to eight in the liver."[1] Bärensprung (quoted by Thierfelder) states that in thirty-three cases of traumatic diseases resulting from injuries of the head, hepatic abscesses were found in six; and Prescott Hewitt, in eighteen injuries of the head, found hepatic abscesses in three and abscesses of the lungs in thirteen.[2]

It would scarcely be proper to make any use of the records of our civil war in this connection, because the constant strain and pressure to which the surgeons both North and South were subjected during those troublous times left them but little time for careful pathological research; but it is not probable that if hepatic abscesses had been of frequent occurrence they would have been overlooked so completely by all the surgeons on both sides; and yet in 12,980 cases of injuries of the head which are reported in the first surgical volume of the *Medical and Surgical History of the War of the Rebellion* I can find no record whatever of an abscess of the liver and but one case which suggests this affection—death being attributed in this to "hepatitis." In addition to this one case of hepatitis, nine of pyæmia are reported, but the seat of the abscesses in these cases is not mentioned.

Of the one hundred and eight cases which I have tabulated for the purposes of the present study there is but one in which it seems in the slightest degree probable that the embolus leading to the hepatic abscess passed through the systemic veins and the hepatic artery to reach this organ. In this case, reported by Harris,[3] a man entered the hospital for an ulcer on the leg; about two months after

[1] Ziemssen's Cyclopedia, vol. ix. p. 99.

[2] Holmes's System of Surgery, vol. i.

[3] Lancet, October 1, 1887.

admission an hepatic abscess formed, was aspirated, and later incised and drained, and the patient recovered.

The occurrence of hepatic abscess in connection with or as a result of malignant endocarditis ought, it would seem, to be of comparatively common occurrence—much more common at least than in those cases where the primary disease is so situated that the embolus has to pass through the lungs before it can reach the arterial system; but, as a matter of fact, very few cases have been reported, so far as I can learn. Thierfelder refers to two—one reported by Mayer and one by Buckling—but the size of the abscesses in these cases is not mentioned. It is probable that this form of cardiac disease runs such a rapid course, and the general symptoms are so pronounced, that the hepatic disease is overlooked before death, and it is also probable that the hepatic abscesses would be of small size and little practical importance. We are justified in concluding, it seems to me, that the occurrence of hepatic abscess from injuries or diseases of the bones, or other parts of the body except those immediately adjacent to the liver, or else directly connected with the portal system of veins, is rare, and the slight danger which formerly existed in such cases has been in great measure removed by the antiseptic or aseptic method of treating wounds.

The conveyance of pyogenic germs or substances by the *hepatic veins* and the consequent formation of abscess in the liver must be extremely rare, if such a thing ever occurs. I can find no cases which seem to have originated in this way, though Younge states[1] that the large single tropical hepatic abscesses are connected with the hepatic veins; the small, multiple ones with the portal veins. There is abundant evidence, however, that the large so-called tropical abscesses are often, if not generally, connected with the portal vessels. Mr. Godlee says:[2] "It appears to be certain, also, that thrombosis and subsequent suppuration may occur in the hepatic veins or their tributaries," but he gives no cases in proof of the statement.

Pyogenic infection through the portal system of vessels is usually considered the most common source of origin of hepatic abscesses, and in a very large proportion of cases which have been carefully studied there seems to have been ulcerative disease of some of the

[1] Medical Press and Circular, August 14, 1889.
[2] British Medical Journal, 1890.

organs connected with the portal system or there was a history of such ulceration at some previous time. Thus, in one hundred and fifty-six cases of acute or chronic catarrhal inflammation of the intestinal mucous membrane *without* ulceration, occurring during our civil war, there was but one cases of hepatic abscess, while there were fourteen cases of multiple abscesses and nine of large single abscesses occurring in five hundred and eleven cases of flux in which the intestine was ulcerated.[1] In a considerable proportion of cases, however, there is no history of previous disease of the intestines or any of the organs connected with the portal system.

Of the one hundred and eight cases which I have studied, there were only forty-seven in which there had been a history of disease of any of these organs, or in which post-mortem examination showed that such such disease had existed; and in one, at least, of these cases the dysentery had existed so long before (eight years) that its connection with the hepatic abscess is *extremely* doubtful. Of the forty cases reported by physicians in this country, eleven were apparently due to disease of the organs connected with the portal system, and in sixteen the cause was unknown; in several of these cases it was distinctly stated that there was no history of diarrhœa, dysentery, or any other disease.

The individual diseases and injuries of the organs connected with the portal system to which hepatic abscess has been attributed are (1) dysentery, (2) appendicitis, (3) gastric and duodenal ulcer, (4) operations on or diseases of the rectum, (5) typhoid fever, (6) suppuration of the umbilical veins in infants, (7) ulceration of cervix uteri, (8) peri-uterine inflammation, (9) suppurating ovarian cysts, (10) lithotomy operations.

Before going further it will be well to call attention to the fact that the word "pyæmic" in connection with hepatic abscess is used differently by different writers on the subject. It is used by some to denote all those abscesses which result from the lodgement of an embolus in the bloodvessels of the liver, and by others it is restricted to those cases which occur in connection with well-marked symptoms of general septicæmia. While it is hard, perhaps, to draw a fast and sharp line between these two classes of cases, it seems to me

[1] Medical and Surgical History of the War of the Rebellion, vol. ii. p. 548.

better, from a clinical point of view, to use the word pyæmic in the restricted sense.

The first fact which strikes one in connection with ulceration of the intestinal canal and hepatic abscess is that all forms of ulceration do not lead to abscess. Sir Dyce Duckworth states[1] that it does not result from either tubercular or typhoid ulceration. As to the second of these he is clearly mistaken, as I shall show a little later on, but I have not been able to find any cases which were clearly due to tubercular ulceration of the bowel. In the case reported by Thorowgood[2] it is probable that the pus-like collections in the liver were really broken down tubercle and not pus. A probable explanation of the circumstance that tubercular ulcers of the bowel do not cause hepatic abscess is to be found in the fact that tubercles are so scantily supplied with bloodvessels.

The ulceration of typhoid fever is a rare source of abscess of the liver. Bernhard reports[3] a case following typhoid fever and terminating fatally, in which the cicatrices of the typhoid ulcers were found at the autopsy. Musser refers[4] to a case in which the intestinal ulcers had healed, but the mesenteric glands had suppurated. It is not easy to understand why hepatic abscess should be so rarely connected with typhoid ulceration. Arnaud advanced the view[5] that it was due to the fact that Peyer's patches are connected with the lymphatics, and that the vessels are comparatively little involved in typhoid fever, but this view is scarcely tenable. Luchtmanns[6] found "follicular ulcers" of the intestines in sixty-one of one hundred and two cases of hepatic abscess, and, furthermore, Peyer's patches are very abundantly supplied with bloodvessels.

Ulceration of the bowel, which often causes dysenteric symptoms, and hence is spoken of as dysentery simply, is usually considered the most common cause of hepatic abscess; but it was frequently remarked, even before the thorough investigations of Councilman and Lafleur, that the dysentery was unlike the common form, and was often mild in character. Younge mentions[7] that dysentery was extremely common during the Crimean war, but only one hepatic

[1] Lancet, April 23, 1887.
[2] Ibid., 1889, ii. p. 268.
[3] Jahrbuch für Kinderheilkunde, 1886, p. 303.
[4] Cyclopædia of Diseases of Children.
[5] Marseille Med., 1887, p. 146.
[6] Quoted by Thierfelder.
[7] Med. Press and Circ., Aug. 14, 1889.

abscess was reported, and he refers also to the statistics of Niemeyer and of Finger, who report three hundred and eleven autopsies in cases of dysentery without finding a single hepatic abscess. Cullimore states[1] that he was informed by Dr. Danford Thomas that he never saw a case of hepatic abscess during his time of service as coroner of London. Sir Dyce Duckworth says[2] that ordinary dysentery does not cause hepatic abscess, and Bartholow[3] makes a similar statement.

In many cases the ulceration of the bowel and the dysenteric symptoms are so mild in character as scarcely to attract attention. Dickinson reports[4] a case in which there was a large hepatic abscess, with no symptoms or history of dysentery, but at the autopsy ulceration of the colon was found. Keiner and Kelsch refer[5] to a case reported by Moxon to the Medical Society of London, in which diarrhœa was present for one day only; death occurred from the opening of an hepatic abscess into a large vein, and at the autopsy a very small ulcer was found in the colon. De Gennes and Kirmisson report[6] a case in which the discharges from the bowels were abundant and glairy in character, and there was but little tenesmus. In many cases, on the other hand, the ulceration of the bowel is deep and extensive, as in the cases described by Councilman and Lafleur.

It is evident, therefore, that so far as ulceration of the bowel is concerned, the hepatic abscess is not due to the character of the intestinal ulceration; and it is almost certain, if not positively established, that it *is* due to the character of the substances formed in the intestinal ulcers, and carried thence to the liver.

There are two or three other questions in connection with hepatic abscess consequent on dysentery which are of interest, namely: (1) How soon after an attack of dysentery commences may hepatic abscess develop? and (2) How long a time must elapse after apparent recovery from dysentery until the danger of hepatic abscess is over?

To the first of these questions a definite answer can be obtained. In the cases of amœbic dysentery reported by Councilman and Lafleur there was distinct evidence of pus formation in the liver in three weeks in two cases and five weeks in one case. Indeed, they

[1] Med. Press and Circular, Aug. 14, 1889.
[2] Loc. cit.
[3] Pepper's System of Medicine.
[4] Trans. Path Soc., of London, 1862.
[5] Archives Gén. de Med., Sept. 1888.
[6] Ibid, 1886, ii. p. 288.

themselves put the time[1] at two weeks in one case, but they say the usual time was from the fourth to the twelfth week. In a case reported by De Gennes and Kirmisson the intestinal trouble occurred early in September and lasted fifteen days; the abscess had clearly formed by September 20th, and was aspirated October 17th. Geschwind reports[2] a case in which three weeks after the first symptoms of dysentery pus was expectorated; a little later a small quantity was aspirated, and then an incision was made through which three-fourths of a litre was discharged. A case almost exactly similar is reported by Barthélemy and Bernardy,[3] pus being obtained on aspiration in three weeks from the commencement of the dysenteric attack, and the case being then treated by free incision, with recovery.

It is extremely difficult—practically impossible, in fact—to say how long a time must elapse after *apparent* recovery from dysentery before the patient is free from the danger of hepatic abscess. There are two obvious difficulties in the way. In the first place, ulceration of the bowel may continue long after the dysenteric symptoms have disappeared, and, secondly, an hepatic abscess may remain latent for an indefinite time. Cullimore states[4] that of twelve cases occurring in his practice in India, dysentery "*immediately preceded*" the abscess in only two. Lamb has reported[5] a case in which a man had dysentery in August, and an hepatic abscess showed itself the following December; but in this case though the dysenteric symptoms had disappeared four months before, the cecum was found ulcerated at the autopsy. Muselier reports[6] a case of multiple abscesses of the liver, in which the man had dysentery in Guadaloupe some months before. In another case the patient had dysentery six months before the abscess appeared, and Olliphant reports[7] a case in which "diarrhœa" occurred a year before.

A case presenting several peculiar features is reported by Guyot:[8]

A man, thirty-eight years old, had suffered with chronic dysentery, but he had apparently recovered three years before the hepatic abscess appeared. In September he was taken sick with indigestion, weakness, pain in the right

[1] Johns Hopkins Hospital Reports, vol. ii. p. 466.
[2] Arch. de Méd. et Pharm. Militaire, 1889, xiv. p. 203.
[3] Ibid., 1890, xv. p. 288.
[4] Loc. cit.
[5] New Orleans Med. and Surg. Journ, February, 1887.
[6] Gaz. Méd. de Paris, November, 1885.
[7] New Orleans Med. and Surg. Journ., May, 1887.
[8] Bull. et Mem. de Soc. Méd. des Hôpitaux, 1886, p. 368.

flank, and gradual emaciation; *he had no fever;* by January there was decided swelling on the right side, and great pain and tenderness; aspiration showed the presence of pus, and a month after one aspiration, at which 1500 grammes of pus were withdrawn, the patient was well.

Quite a number of cases have been reported in which dysentery preceded abscess formation by several years; thus, O'Donnell,[1] after stating his belief that ulceration of the bowel is a rare cause of hepatic abscess outside the tropics, mentions a case in which dysentery preceded the abscess by nine years; and Faunce and Rowan report[2] a case of abscess occurring eight years after dysentery. At first sight one would suppose that there could be no possible connection between the dysentery and the hepatic abscess in these cases, nor is it probable that there *was* any connection, but it is certain that ulceration may exist in the bowels for a long time after apparent recovery from dysentery, and an hepatic abscess may remain latent for a long time certainly, but just how long is not known.

Another interesting fact just here is that dysentery may recur in the same person one or several times after an interval of several months or even several years. A case of this kind has recently come under my observation.

A gentleman was taken in the autumn of 1881, after a visit to a marshy section of Virginia, with a severe attack of dysentery; he recovered in a few weeks' time, but in 1884 and in 1888 he had similar attacks. In January last he was again attacked, and I saw him in consultation in February. An examination of the discharges, made by my colleague, Prof. Tuttle, showed that they contained amœbæ. The case ran a tedious course, but finally ended in recovery.

The entrance of pyogenic substances into the liver by the *lymphatics* is of questionable occurrence; but it seems to me highly probable that the frequent extension of such abscesses into the adjacent pleura and lung may occur through the lymphatic vessels of the liver, "which communicate with the thoracic lymphatics through the triangular ligament and suspensorium."

Suppuration may occur around the *bile-ducts* and lead to abscess formation from several different causes: (1) Retention of bile;[3] (2)

[1] Med. Press and Circular, June 19, 1889. [2] Indian Med. Journ., 1888, p. 539.

[3] Godlee says the simple distention of the bile-ducts does not cause abscess; that it only occurs when some foreign body, such as a gall-stone, or a worm, causes ulceration of the duct.

the presence of gall-stones; (3) the entrance into the ducts of intestinal worms; (4) probably, also, from an angiocholitis of unknown origin. Cases of this character do not seem to be very common when compared with the total number of hepatic abscesses reported, but if so-called tropical abscesses be left out they are probably comparatively common. Musser has collected seven cases in which the abscesses were caused by round worms, and other cases have been reported. One of the most remarkable was reported[1] by Bates a number of years ago.

A negro child, three years old, was taken with violent pain in the belly, paroxysmal in character and very severe; there was great tenderness over the region of the liver, and the organ was somewhat enlarged; the child lived nine days. At the autopsy two abscesses were found in the liver, one of which contained one and one-half ounces of pus; in addition to these abscesses, however, forty-two round worms were found in the substance of the liver, and similar worms were found in the intestines.

Of thirteen cases of multiple small abscesses collected by Carrington,[2] three were due to obstruction to the outflow of bile. Leyden also reports[3] a case of multiple small abscesses due to gall-stones, and a similar case is reported by Harris.[4] In Harris's case there were many small abscesses in the pancreas, as well as in the liver. So far as I can learn from the reported cases, abscesses which originate from trouble about the bile-ducts are usually small in size and multiple, but this is not always the case. Polaillon[5] reports a case of very large single abscess beginning as an angiocholitis, and Kermisson,[6] one due to gall-stones in which there was one large and several small abscesses. The abscesses were in the right lobe. The biliary canals were "enormously dilated," the pus was thick and yellow, the wall of the abscess dark, and small bloodvessels opened into the abscess; there was also a small abscess in the right lung.

Spread of suppurative inflammation from adjacent parts or organs may occasionally induce hepatic abscess. Beckham has recorded[7] a case in which an abscess originally between the abdominal wall and liver, or possibly in the abdominal wall, extended to the liver, and caused

[1] New Orleans Med. and Surg. Journ., March, 1846.
[2] Guy's Hosp. Reports, vol. xxvi.
[3] Charité Annalen, 1886.
[4] Indian Med. Journ., 1885, p. 603.
[5] Gazette Méd. de Paris, June 18, 1887.
[6] Bull. Soc. Anatomique, 1873, p 674.
[7] New Orleans Med. and Surg. Journ., 1867, p. 67.

erosion or ulceration of its outer surface; there was a fistulous opening into the sac, through which pus and fragments of hepatic tissue were discharged. Councilman and Lafleur think it probable that there was a direct passage of amœbæ from the colon to the liver in some of their cases of amœbic dysentery. In the cases where it was supposed to result from pneumonia, it is more probable that the abscess was the primary condition, and the pneumonia resulted from it.

Injuries of the liver lead to hepatic abscess in a considerable number of cases, and these injuries may be penetrating wounds, simple contusions without external injury, or they may cause fracture of the ribs, and lead to hepatic abscess, and possibly cause hepatic abscess secondarily. I can find but three cases of hepatic abscess from penetrating wounds of the liver, reported in the *Medical and Surgical History of the War of the Rebellion*. One of these was from a punctured sabre wound, and the other two from shot injuries. In each case the abscess resulted very soon after the receipt of the injury.

As a rule, the abscesses due to other forms of injury, such as blows, appear in a few days. Eight of the one hundred and eight cases in the table were clearly due to injuries, and in these cases the interval from the receipt of the injury to the appearance of the abscess varied from four to thirteen days. Thus Barthélemy and Bernardy report[1] a case in which the abscess appeared four days after a blow; Tournier,[2] one four days after a blow on the belly and exposure to cold; Barth,[3] one in which the liver was enlarged in three days, though pus was not aspirated for three months; Siredey,[4] one in which a man received a kick from a horse, and pus was present in eight days, and Weir,[5] one in which, after a fall on the buttocks, an hepatic abscess formed in thirteen days. In two cases the interval between the injury and the abscesss formation is not stated, and in three, while the abscesses were supposed to have been due to injury, the evidence is by no means conclusive.

I shall have but little to say about the general or local conditions

[1] Archives de Méd. et Pharm. et Militaire, 1890, xv. p. 285.
[2] Provence Médicale, November 22, 1890.
[3] Bull. Soc. Anatomique, 1856, p. 111.
[4] Ibid., 1858, p. 499.
[5] New York Med. Record, April 29, 1882.

which are favorable to the development of hepatic abscess. A *hot climate* is universally considered a potent factor, but it is quite evident that it is not the *heat* simply which is the active agent, because the disease is not equally common in all hot countries. Perhaps the chief action of heat is in furnishing one of the conditions requisite for the growth and development of amœbæ ; it is probable that those abscesses which are so greatly influenced by climatic conditions are amœbic in character. Harley[1], Cullimore,[2] and Younge[3] think chilling of the body when overheated a potent cause, and Cullimore claims that horseback riding is liable to induce it.

There is much difference of opinion with respect to the influence of *malaria*, but the weight of evidence seems to be clearly against any connection between the two diseases. Cullimore, Keiner and Kelsch, Dutrolau—in fact, nearly all writers on tropical affections—deny such a connection. Blanc,[4] on the other hand, considers malaria a powerful predisposing cause, and Tomes[5] thinks malaria a frequent attendant on hepatic abscess. The rarity of hepatic abscess in those sections of the eastern part of the United States where malaria prevails furnishes strong presumptive evidence against any connection between the two diseases ; but Bartholow states that hepatic abscess is common in the Mississippi Valley, and of twenty cases occurring in the St. Louis Hospital reported by Robinson,[6] in ten "intermittent fever," "chills and fever," or "chills" are mentioned as causative or complicating conditions. In seven of the ten cases, however, dysentery or diarrhœa had preceded the abscess ; in two of the other three cases the chills and fever occurred during the time the abscess was forming, or after it had formed, and in the other there had been no chills for four years until about six weeks prior to the appearance of the abscess.

Mr. Godlee, in his lectures on the "Surgical Aspects of Hepatic Abscess," states his belief that malaria is sometimes connected with abscess formation in the liver. It seems to me probable that the only real connection between malaria and hepatic abscess is to be found in the fact that the same conditions are favorable for the

[1] Med. Press and Circular, February 3, 1886.
[2] Ibid., November 30 and December 7, 1887.
[3] Ibid., August 14, 1889.
[4] Lancet, February 20, 1886.
[5] Ibid., October 9, 1886.
[6] St. Louis Courier of Medicine, January, 1879.

development of the plasmodium malariæ and the amœba of amœbic dysentery. Possibly malaria may weaken the resisting power of the liver, and thus act as a predisposing cause also.

Intemperance is universally recognized as a predisposing cause of hepatic abscess in India, and it is probable that it is elsewhere. It is worthy of note, too, that even "moderate drinkers" are very liable to the disease in India. Hatch[1] reports seventeen cases; of these, seven used liquor to excess, and nine were moderate drinkers.

With respect to *age and sex*, adult males are far more liable to hepatic abscess than children or women. Chiefly, perhaps, because they are more exposed to the predisposing and exciting causes; but young people are by no means as exempt from this affection as was formerly supposed. Musser[2] has collected thirty-four cases in persons under fifteen years old, and many other cases have been reported. Thus Hill records[3] the case of a boy nine years old, who had suffered from repeated attacks of periodical fever, in whom an hepatic abscess developed. It was incised and drained, and discharged nearly half a pint of greenish pus. McClelland reports[4] the case of a girl eight years old, who swallowed a pin fourteen months before, and "about that time" had pain in the right groin; the case terminated fatally, and at the autopsy, one abscess the size of an orange, and many smaller ones were found in the liver, and one in the brain. A case is also reported[5] by Pereira in a child twenty months old who had dysentery in November, and the abscess appeared in the following December. Janeway has also reported[6] a case in a child three years old, and the case reported by Bates in a child of three years, has already been alluded to.

The usual *seat*, the *number*, and the *size* of hepatic abscesses are points of great practical importance with respect to prognosis and treatment. The usual seat of an abscess is in the right lobe, and even when the abscesses are multiple, the right lobe is chiefly involved. Furthermore, it would seem that the *upper* part of the right lobe is involved rather more frequently than the lower part.

With respect to the number of abscesses, it is hard to get definite information. Of the 108 cases which I have studied there were

[1] Lancet, January 5, 1889.
[2] Cyclopædia of Diseases of Children, vol. iii.
[3] Indian Med. Journal, 1887, p. 204.
[4] Lancet, April 10, 1886.
[5] Indian Medical Gazette, June, 1890.
[6] Trans. New York Med. Assoc., 1884.

multiple abscesses in 42 cases; while in 55 there was but 1; in 11 cases the number of abscesses was not stated. In those cases which complicate general septicæmia, it is quite certain that the abscesses are in the great majority of cases multiple in number and small in size, but these cases are of little *practical* interest at any rate, and it is of far more importance to determine, if possible, the size and number of the abscesses in those cases which offer some hope of relief from remedial measures.

Of the 8 cases in which the disease was *clearly* due to injury, there was but *one* abscess in 4 cases; in one there were 2; and in one 6; and in one (Siredey's case) "many;" in the other the number is not mentioned, but it would appear from the context there was but 1. Of the 4 cases *probably* due to injury, in 2 there was but 1 abscess; in 1 there were several; and in 1 the number is not stated.

Of the 31 cases in which there was a history of either dysentery or diarrhœa, or in which ulceration of the large bowel was found, at the autopsy, there were multiple abscesses in 15 cases. In 14 cases there was but 1, and in 2 the number is not stated. Of 38 cases in which the cause of the abscess could not be discovered, 27 were single, 9 multiple, and in 2 the number was not stated. Eighteen of these 38 abscesses were reported in the United States, and of the 18, 15 were single, 2 multiple, and in 1 the number was not stated. Twelve were reported by French physicians, and of the 12, 4 were multiple. Eight were reported by English physicians, and of these 4 were multiple and 4 single.

One of the American cases reported here as one of multiple abscesses presented peculiar features. It is reported by Schoolfield in the *Cincinnati Lancet and Clinic* for December 28, 1889.

In this case there were four abscesses, but they appeared at different times. The first burst into the lung, and a month after apparent recovery another abscess appeared, which was incised and drained, in two weeks. Recovery seemed to be complete in a month's time, but two months after the second apparent recovery, a third abscess appeared, which was incised and drained in three weeks' time; recovery was slower then and was only complete after four months. Two months later still the abscess recurred for the fourth time, broke into the lung and abdominal cavity, and caused death.

A somewhat similar case of recurrent abscess has been reported by Rosemont-Malbot.

The first abscess in this case broke and recovery ensued; a second appeared twenty months later, was incised and drained, and the patient was well in forty days; five months later a third abscess appeared and was incised, but general peritonitis supervened and terminated fatally.

Of 8 cases of abscess due to obstruction of the bile-ducts, 7 were multiple and 1 single, and it is questionable whether that was actually located on the liver. In only 1 of the cases was there a large abscess. Carrington has reported a case in which there were two large and many small abscesses, and he considered the combination very rare; but this view is clearly erroneous, as 7 other cases appear in the 108 which I have collected, in which there were one or two large, with many smaller abscesses in the same liver.

The relation of multiple abcesses to each other is a matter of direct and practical importance. In a general way it may be stated, perhaps, that the longer a case lasts the greater the probability that multiple abscesses will open into each other, but this fact does not, of course, justify delay in surgical treatment, because the longer the duration the greater, as a rule, is the destruction of hepatic tissue, and the greater is the danger of exhaustion or of the bursting of the abscess in some unfavorable direction. That the presence of one or more additional abscesses may cause death, after one has been opened and drained, there can be no question. Ferron, for instance, reports[1] 47 cases of antiseptic hepatotomy for abscesses, in 8 of which the abscesses were multiple. Of the multiple cases 5 terminated fatally, while there was but 1 death in the 39 cases of hepatotomy in which the abscess was single.

Tournier has also reported[2] an interesting case of hepatic abscess due to injury, the presence of pus being evident four days after the injury was inflicted. One abscess in this case was opened by Vienna paste and incision, but the case terminated fatally, and at the autopsy another abscess was found which had not been opened. A somewhat similar case is reported by Arnaud,[3] in which the patient died twelve days after incision into one abscess; at the autopsy the abscess was found healed, but there was another present which had caused death.

Sometimes—how often I have not been able to learn—a second abscess will burst into the one which has been opened. Thus,

[1] Gazette hebdom. de Sci. Méd. de Bordeaux, 1887, p. 159.
[2] Provence Médicale, November 22, 1890.
[3] Marseille Méd., 1887, p. 146.

Cliquet reports[1] a case in which an abscess was incised and drained; there was temporary improvement, but fever, sweats, pain, and prostration recurred. Twenty-four days after the incision there was a sudden and profuse flow of pus, with immediate relief. It seems to me highly probable that the bursting of a second abscess into the cavity of one which has been opened must be of comparatively common occurrence, because the recoveries from hepatic abscess, when one sac only has been opened, are relatively much more frequent than single abscesses.[2]

I shall have but little to say about the *contents* of an hepatic abscess, but there are two or three practical points which it may be well to mention. The first of these relates to diagnosis. It seems to be generally held that aspiration is quite a certain means of detecting the presence of pus, but this is clearly a mistake. Councilman and Lafleur mention the fact that in some of their cases of amœbic abscess the contents were so thick that they would not flow through an aspirator needle, and in a case which I saw in consultation a year or two ago the contents of the abscess had undergone caseous degeneration, and aspiration gave a negative result.

It would be interesting to determine how long it takes for pus in the liver to undergo this caseous change, but there are hardly any facts which throw light on this point. Nor would it be easy to determine it at any rate, because of the frequency with which abscesses are latent. In the single case which I have seen, it was about six weeks from the time the first symptoms of abscess appeared till aspiration was attempted.

The second point of practical interest in connection with the contents of an hepatic abscess is the frequency with which the contents are sterile. "Bacteria were found in 3 of the 6 cases" reported by Councilman and Lafleur. Laveran has reported[3] 2 cases which were sterile, and Netter, in the discussion following the reading of Laveran's paper, stated that of 13 cases of amœbic dysentery, Kartulis had found 8 sterile; of 9 cases of "idiopathic abscess of hot countries" 4 were sterile. He expressed the opinion, too, that the

[1] Archiv. de Méd. et Pharm. Militaire, 1886, i. 299.

[2] In a case of amœbic abscess operated on since this paper was written a second abscess burst into the cavity of the first five weeks after incision, and a week later a third burst in the same direction; the patient is still under treatment.

[3] Bull. et Mém. de Sci. Méd. des Hôpitaux, 1890, p. 691.

sterility was due to the long time the abscess had lasted—an opinion which is scarcely tenable in view of the rapid course of some of Councilman and Lafleur's cases.

Peyrot[1] has reported a case in which pus from an hepatic abscess of unknown origin escaped into the peritoneal cavity without any subsequent trouble, and he attributes the absence of peritonitis to the sterility of the pus. This sterility of the pus, or its *possible* sterility, might furnish a crumb of comfort when pus *did* escape into the abdominal cavity; but it would certainly not justify the failure to prevent such contamination as far as possible.

The presence of liver-cells in the contents of an hepatic abscess does not seem to be of very common occurrence. It is mentioned in 8 of the 108 cases. Occasionally their presence is of great value in diagnosis. A few years ago I saw a gentleman from Cincinnati, who was supposed to be suffering from phthisis. At my first visit I found he had been taken a few hours before with profuse discharges of yellowish matter from his bowels. On microscopic examination these were found to consist of pus and fragments of hepatic tissue and liver-cells.

The condition of the walls of the abscess and the surrounding hepatic tissue depends in great measure on the duration of the abscess. In the very early stages there is no very sharp line of demarkation, but later on, the walls are distinct and ragged; still later, they may be thick and fibrous, and Haspel (quoted by Frerichs) states that the fibrous wall may be formed in twenty or twenty-five days; but it is evidently very hard, if not impossible, to say how long a time is necessary for this change in the wall to occur, for abscesses having such fibrous walls pursue a tedious course, and are often latent.

The surrounding tissue is often sound, but it may be fatty, as in cases reported by Dymock[2] and Arnaud.[3]

The changes in the neighboring parts and organs are of great practical importance, especially the presence or absence of adhesions.

In 30 of the 108 cases which I have tabulated, the presence of adhesions is mentioned. In 8 it is mentioned that there were *no* adhesions. In 70 cases no mention is made of adhesions, one way or

[1] Bull. et Mém. de Sci. de Chirurg., February and March, 1891.
[2] Indian Med. Gazette, 1866, p. 298.
[3] Marseille Méd., 1887, p. 146 et seq.

the other. In 11 of the 30 cases the abscess was due to dysentery, and in 7 of the 11 cases there were multiple abscesses. In 16 cases the cause of the abscess was unknown, and in 5 of these there were multiple abscesses. Adhesions were mentioned in only 1 case, when the abscess was due to injury, and then the adhesions were between the liver and the diaphragm. In 20 of the 30 cases the liver was adherent to the abdominal walls.

A comparison of the symptoms present in those cases where adhesions existed, and in those where there were *no* adhesions, does not indicate any means by which their presence or absence may be determined. Cliquet[1] thought that œdema of the abdominal walls over the seat of the liver was an evidence of adhesions having formed, but this view cannot be substantiated. The presence of this symptom is noted in only 2 of the 30 cases, and Ramonet has reported[2] a case in which this symptom was present, and in which he distinctly states adhesions were not present. In 1 other case, however, not included in the 30, where adhesions certainly existed, there was extreme œdema of the skin, and adhesions probably existed because there was necrosis of the ribs in this case.

The *symptoms* of hepatic abscess are usually quite well marked, but are sometimes obscure and occasionally there are no symptoms pointing to hepatic disease. Thus, Woolbut records[3] a case in which a laboring man, in apparently perfect health, was suddenly seized with severe pain in the abdomen, followed by collapse, and terminating in death in a few hours' time; he had received no injury of any kind and had not had dysentery; at the autopsy, the left lobe of the liver was found ruptured, and in the right lobe were found one large and several small abscesses, the presence of which had never been suspected.

McLean[4] speaks of a case in which a man died of phthisis, who had never presented any symptoms of hepatic trouble, but at the autopsy a cavity the size of a walnut, and containing a rusty needle swallowed two years before, was found in the liver; the abscess-cavity opened into the duodenum and drained in that way. He mentions also another case, in which a man with "no previous history of disease" walked seven or eight miles in search of work; soon afterward

[1] Loc. cit. [2] Archives de Méd. et Pharm. Militaire, 1889, p. 321.
[3] Indian Med. Gazette, December, 1886. [4] Reynolds's System of Medicine.

he complained of sudden pain, became collapsed, and died in a very short time. At the autopsy a large abscess with very firm walls was found which had suddenly burst into the pericardium.

Even close adhesions to surrounding parts may form apparently without giving rise to any symptoms; thus Rohé reports[1] a case in which a woman died quite suddenly with pneumonia; there had been no hepatic symptoms during life; but at the autopsy an abscess holding four ounces was found in the liver, which contained several gall-stones, and was adherent to the stomach, pancreas, duodenum, and gall-bladder. Tournier (*Provence Méd.*, November 22, 1890) reports a case also in which there were no symptoms pointing to the liver, but in which, at the autopsy, an hepatic abscess was found, and the organ was found closely adherent to the abdominal wall.

McLean expresses the opinion that those cases which present no symptoms are very chronic in course, and the abscesses have thick walls, but this is not always the case. Souques has recorded[2] a case following old perityphlitis, which presented no symptoms pointing to the liver, but which ran a rapid course, and caused death before rupture of the abscess.

The *onset* of the symptoms in most cases of hepatic abscess is gradual, but now and then very sudden. Thus, in a case reported by Ferrand,[3] the patient was taken suddenly with violent pain in the abdomen, and vomiting; he was constipated, but an enema brought away black, offensive matter; the symptoms continued; fever supervened, and the liver became moderately enlarged; death occurred in a month's time, and at the autopsy a number of abscesses, from the size of a bean to that of a pullet's egg, were found, containing grumous muco-pus; the walls were blackish and gangrenous, and there were adhesions to adjacent parts.

Of the usual symptoms of pus-formation—*rigors, fever and sweating*—fever was present in a very large proportion of the cases. Its presence is distinctly mentioned in 61 of the 108 cases; there was said to be an absence of fever in 5 cases, in which other symptoms of hepatic abscess were present, but the records are not sufficiently full to be satisfactory on this point. I am at this time attending a case in consultation, in which there is no fever during the day, but at

[1] Med. and Surg. Reporter, November, 1881.
[2] Bull. Soc. Anatomique, 1889.
[3] Bull. et Mém. de Soc. Méd. des Hôpitaux, 1887, p. 496.

night a rise followed by sweating. The temperature, except in cases which ran a very rapid course, did not usually rise above 102.5° or 103° in the afternoon, and in the morning was often normal; the temperature elevation, furthermore, in most cases occurred at irregular times. In 44 cases no mention is made of fever, but it is probable that it was present in most of the cases at least.

The occurrence of *rigors* is mentioned in 14 cases only, and sweats are said to have occurred in only 9. Doubtless, in many cases, both the rigors and the sweating were overlooked, but in quite a number of cases it is distinctly stated that they were absent.

Jaundice seems to be present, so far as can be judged from the limited number of cases which I have analyzed, more frequently than is commonly supposed. Its presence is mentioned in 11 of the 108 cases. In two of these cases the jaundice was very slight, however; in one of them there were no adhesions present, and in the other it is not stated whether adhesions were present or not. Of the 9 remaining cases, in 4 there were more or less dense adhesions surrounding the liver or connecting it with adjacent organs; and in the other 5 the jaundice was due to the presence of gall-stones, or other obstruction of the duct, which had given rise to the hepatic abscess. It seems to me highly probable, therefore, that in most cases of hepatic abscess in which jaundice is present, this latter symptom is due not to the abscess itself but to pressure on the bile-ducts by adhesions, or to obstruction by gall-stones. An *earthy tint* of the skin is mentioned by many of those who have reported cases of abscess of the liver as of common occurrence.

Ascites is reported as present in 6 cases; in one of these the probable cause was suppurative portal phlebitis; in 4, more or less dense adhesions were present, and in 1 the presence or absence of adhesions is not mentioned.

The *digestive* symptoms are variable. There is usually complete loss of appetite, but occasionally it remains good. *Nausea* and *vomiting* were noted in 13 of the 108 cases, and in only 6 cases was their absence specifically mentioned. *Diarrhœa* was present in 18 cases, and constipation in 10. In 2 cases there was alternate diarrhœa and constipation. In 1 case it is distinctly stated that the bowels were regular. It is evident, therefore, that the condition of the bowels is of but little value as a symptom of hepatic abscess.

Disturbance of the *nervous system*, except pain and tenderness in the region of the liver, which will be considered hereafter, is rarely mentioned. The occurrence of headache is mentioned in 3 cases, delirium in 2, and stupor in 1. No doubt in many cases there were nervous and other symptoms, which are not mentioned by the reporters of the cases; but if these symptoms had been conspicuous, it is scarcely probable that they would have been omitted.

Disturbances of the *circulatory system*, except ascites and weakness of the pulse, are very rarely mentioned. In 1 case there was enlargement of the superficial veins of the abdomen; the abscess in this case supervened "very shortly" after a blow over the liver; the patient lived three months, and at the autopsy the liver was found adherent to the diaphragm on the right side; there were no abdominal adhesions; there was some effusion (serous) in the left pleural and in the pericardial sacs. In another case there was repeated epistaxis, and in a third the pulsations of the heart were communicated to the abscess.

Disturbances of the *respiratory system* are quite common. *Dyspnœa* is mentioned as a troublesome symptom in 12 cases, and *cough*, which was not usually very troublesome, however, is mentioned in 8 cases. The existence of râles, usually subcrepitant, is mentioned in a few cases, and occasionally pleuritic friction-sounds were observed. There would seem to be several causes for the disturbances of respiration in cases of hepatic abscess: (1) The pain occasioned by breathing; (2) the pressure of the abscess upward upon the lung; (3) the bursting of the abscess into the lung; (4) the bursting of the abscess into the pleural cavity; and (5) the existence of pleurisy (which may be serous) as a complication.

Disturbances of the *urinary system* are mentioned but three times in the one hundred and eight cases. Once the presence of albuminuria (five per cent.) was noted. The cause of the abscess in this case was supposed to be a wound by a pistol-ball received two years before. It is worthy of note that the spleen was enlarged in this case. The abscess was incised and drained, and the case ended in recovery. In view of the small amount of albumin present and the extreme rarity of the complication, it is probable that its presence was not connected in any way with the hepatic abscess. In only two cases, so far as I can learn, was any careful examination of the urine

made to determine the amount of urea present. Both of these cases are reported by Arnaud,[1] and in one one hundred and thirty-five grains of urea were discharged per day; in the other, one hundred and twenty-three. The amount of the other constituents of the urine is not stated, nor is any statement made with respect to the presence or absence of leucine and tyrosine.

Emaciation is probably present, in greater or less degree, in nearly all cases, though it is only mentioned specifically in twenty-one of the one hundred and eight cases; in some cases, however, it is absent. In a case which I saw a few years ago there was scarcely any loss of flesh, and the thick layer of adipose tissue on the back prevented us from detecting the enlargement of the liver, which was in the back part of the right lobe. Rouis, quoted by Frerichs, says that in three cases he had seen great increase of adipose tissue.

The evidence furnished by a *physical examination* of the liver is of far more value than the symptoms in cases of hepatic abscess. Of the eighty-nine cases in which the symptoms are given in some detail, *pain and tenderness* are mentioned as prominent in fifty-six; in four there was tenderness without pain; in two there was complete absence of both pain and tenderness; in the others no mention is made of pain one way or the other. The character of the pain varies: sometimes it is quite steady; at others it occurs in paroxysms. The seat of the pain is also different in different cases, and seems, as a rule, to depend upon the direction in which the abscess is pressing; if it is pressing upward against the lung, the pain is usually under the right scapula or in the right shoulder, though this does not always occur. Thus, in a case reported by Arnaud, the abscess pushed the lung upward very considerably, and yet there was no pain in the shoulder or scapular region. If, on the other hand, the abscess is on the under or front surface of the liver, the pain is usually in the epigastric or hypochondriac region. We have already seen, however, that pain may be entirely absent in such cases, even where adhesions have formed or are forming.

Enlargement of the liver, to a greater or less degree, is present in nearly all cases; it is usually sufficiently great to be plainly evident on palpation and percussion. Of the eighty-nine cases in which the

[1] Loc. cit.

symptoms are mentioned in detail, enlargement was named in sixty-three, and it was probably present in nearly all the others, for in some of them fluctuation is mentioned, and in some aspiration was practised and revealed the presence of pus. In three cases the enlargement was said to be slight; in two of these three cases the abscess was due to dysentery which had first appeared in one case two weeks and in the other three weeks before the abscess became apparent, and was incised. In the other case it was due to a blow; the abscess symptoms appeared four days after the injury, and incision was practised twenty-eight days after. In two cases it is distinctly stated that the liver was not enlarged; one of these cases was due to dysentery, and the abscess itself was large and single; in the other there were multiple abscesses following obstruction of the bile-duct. In one case attributed to alteration of the cervix uteri the liver was contracted by "fibroid material."

The situation of the enlargement depends on the part of the liver involved; in the great majority of cases it is on the right side, and it seems to pass upward into the chest and downward into the abdomen in about an equal number of cases. Sometimes, when the swelling can scarcely be perceived or even felt—owing to the tension of the muscles—when the patient is lying down, it becomes very evident when he stands or sits up, the epigastrium and the right hypochondrium then bulging out very markedly; this occurs even when there are close adhesions, as in a case I have recently seen. In the case of very large abscesses the swelling may extend down to the crest of the ilium, as in a case in my own practice, which I have heretofore mentioned, and in a case reported by Hazzard, in which the enlarged liver extended upward to the third rib and downward to four inches below the ribs.

Fluctuation was only mentioned in eight of the cases which I have tabulated; and in very many cases, no doubt, it is absent in consequence of the distance of the abscess from the surface, or obscured by the condition of the abdominal walls or by tympany.

Aspiration is spoken of by most writers on the subject as a certain test of the existence of an hepatic abscess, and in the great majority of cases, certainly, in which it has been tried, pus has been withdrawn, if it was present. But there are two conditions, at least, in which pus may be present and aspiration fail to reveal it: (1) The

needle may not enter the abscess; (2) the contents of the abscess may be so thick that they cannot flow through the needle. This fact has been previously mentioned in speaking of the contents of hepatic abscesses, and need not be dwelt upon now further than to say that it would seem that the contents of dysenteric abscesses, and it would perhaps be fair to say those due to amœbic dysentery, are sometimes thick at a very early period. In addition to the cases mentioned by Councilman and Lafleur, in which aspiration gave a negative result, Geschwind reports one due to dysentery, which preceded the abscess by only two weeks, in which very little pus was aspirated, though three-fourths of a litre was discharged on incision. I do not find any record of a failure to get pus when the needle entered the abscess in any except dysenteric cases, unless the abscess was of old date and its contents had undergone caseous degeneration.

The *complications* of hepatic abscess are quite numerous, but with the exception of dysentery, localized peritonitis and consequent adhesions, and those connected with the pleura and lungs, they are rare.

The *dysentery*, which is such a frequent complication of the amœbic abscesses, has already been described very fully by Dr. Councilman, and I shall not refer to it.

Nor is it necessary to say much with respect to *peritonitis*. We have already seen that in quite a considerable proportion of cases this complication exists, but in the great majority it is localized and adhesive, and so far from being a harmful matter, it is clearly beneficial when there are adhesions to the abdominal wall, because it removes to a great extent the dangers of an escape of pus into the abdominal cavity when the abscess is incised. In the same way, also, adhesions to the hollow viscera lessen the gravity of a case in which pus is discharged into the alimentary canal. Occasionally, however, a *generalized peritonitis* is found which is not due to the rupture of the abscess into the abdominal cavity. Thus in a case reported by Ridlon,[1] due to ulceration of the bowel, there was a generalized chronic peritonitis, and the abdomen contained sixty ounces of fluid; and Hazzard[2] reports two similar cases, one due to dysentery, the cause in the other unknown.

Hemorrhage from the bowels, or rather hemorrhage *into* the bowels

[1] New York Med. Journ., April, 1880.

[2] Med. and Surg. Reporter, Jan. 21, 1882.

from the cavity of the abscess, is a very rare and very dangerous complication, apparently—that is, if any amount of blood is discharged; in many cases in which the abscess bursts into the colon there is a slight discharge of blood along with the pus, but this slight hemorrhage is only incidental to the rupture, and is not worth calling a complication.

Pleurisy is one of the most common of the complications of hepatic abscess; its occurrence was noted in 11 of the 108 cases. In most cases the exudate was purulent in character, and was then usually due to the rupture of the abscess into the pleural sac, but in some cases the exudate was serous; cases of this kind are reported by Hazzard,[1] Feron and Constan,[2] and Arnaud.[3]

Pneumonia is also an exceedingly common complication, as is apparent from the frequency with which hepatic abscesses burst into a bronchus; in all such cases there is a pneumonia of greater or less extent, but it does not seem to add to the gravity of the case as a rule; on the contrary, recoveries after rupture into a bronchus are more frequent than after ruptures in any other direction.

Infarction of the spleen is rarely mentioned as a complication of hepatic abscess, and it is of little practical significance at any rate.

Meningitis is also a rare complication, so far as I can determine from the reports which I have examined; it is not mentioned in any of the one hundred and eight cases which I have analyzed, though in one of them there was an abscess of the brain. Perhaps meningitis may have been a more common complication formerly, when injuries of the head were said to be a common cause of hepatic abscess.

Caries of the ribs has been noted in several cases. Thus Chauvel[4] reports two cases of this kind, and Byrd has recorded[5] a case of unknown origin in which there was "necrosis of the ribs." The abscess had lasted about nine weeks when this was detected; it was very large, and there was œdema and redness of the skin over an extensive area. A very remarkable case has been reported by Hatch[6] in which the whole side sloughed away, and not only the carious ribs, but the

[1] Loc. cit.
[2] Gazette hebd. de Sci. Méd. de Bordeaux, March 6, 1889.
[3] Loc. cit.
[4] Gazette des Hôpitaux, 1890, p. 91.
[5] New York Med. Journ., July, 1878.
[6] Lancet, January 5, 1889.

kidney was also exposed. An hepatic abscess may terminate in several different ways.

Absorption is said by some writers on the subject to be of occasional occurrence, but I can find no case of the kind recorded which is at all conclusive. In fact, the term "absorption" has been used sometimes, not to signify the complete disappearance of the pus, but to include its cheesy and calcareous degeneration as well. Thus Frerichs says that in most cases where absorption occurs, a cheesy or calcareous remnant remains. Now this is clearly not absorption in the proper sense of the word, and it does not seem to me proper to include those cases under this heading.

Bursting of the abscess is of comparatively common occurrence. Its actual frequency cannot readily be determined, especially since the propriety of early incision has been recognized, but the statistics of Waring will throw some light on this point. Of the 300 cases analyzed by him, 78 opened spontaneously, 48 were opened artificially, 169 died before bursting or incision, and in 5 the result in this respect was doubtful.

Of the 108 cases which I have analyzed, rupture occurred in 18, 26 died before rupture, and aspiration or incision was done in 59 cases; in 5 there is no distinct record on this point. In addition to the 26 cases in which death occurred before rupture, there were 2 in which one abscess had been incised and drained, but at the autopsy another abscess was found, which had not been opened. One patient had abscesses four different times, two of which burst, and two were incised and drained. Another had three different attacks; in the first the abscess broke, the second was incised and drained, and the third was incised, but peritonitis came on and caused death. The interval between the first and second abscess was twenty months, that between the second and third five months.

The direction of the rupture in the eighteen cases was as follows: Into a bronchus seven times, into the pleura four times, into the colon three times, into the stomach twice, into the abdominal cavity three times, outward through the abdominal walls once, and into the pericardium once. In one case rupture occurred both into the bowels and a bronchus, and in another it occurred into the lungs and peritoneal cavity; in yet another into both the pleural cavity and a bronchus. All the four cases in which the abscess broke into a

bronchus only, ended in recovery, and recovery ensued also in the cases in which rupture occurred into a bronchus and the pleural cavity, and a bronchus and the bowel, respectively. Three of the four cases in which rupture occurred into the pleura terminated fatally; in the only one having a favorable termination there was an opening into the bronchus also. Of two cases in which the abscess opened into the bowel only, both died; the third, which opened into a bronchus also, ended in recovery. Both the cases which opened into the stomach terminated fatally, and all three of those which opened into the abdominal cavity had a similar ending, as would have reasonably been supposed. It will be remembered, however, in this connection, that in one case in which pus escaped into the abdominal cavity when the abscess was opened, recovery ensued.

These cases are too few in number to justify very positive conclusions as to the frequency and gravity of rupture of an hepatic abscess in different directions, but I think one conclusion is fully justified, namely, that rupture into a bronchus, or, as it is often called, rupture into the lung, is the most common and least dangerous direction in which such rupture may occur.

Caseation and *calcification* of its contents are very rare terminations of an hepatic abscess, and are not mentioned in any of the 108 cases which I have analyzed.

Death is a direct result of hepatic abscess in a large proportion of the cases. Of the 108 cases in my table, 67 terminated fatally—of this number 21 had been either aspirated or incised or drained. 43 cases terminated in recovery, and of these 38 had been either aspirated or incised. The result in three cases is not stated. It will be observed that the total number of *patients* is 108, but the total number of abscesses is 110. This result is due to the fact, previously mentioned, that one patient had three separate and distinct attacks, and another had four. There were two cases, however, in which the result is not stated. Of the 69 fatal cases, the abscesses were multiple in 39 cases, single in 24, and in 4 the number is not stated. If we compare these figures with the general proportion of multiple to single abscesses—42 of the former to 55 of the latter—it is evident that the mortality is much greater in the cases of multiple than of single abscesses.

The causes of death are: (1) Exhaustion; (2) septic poisoning;

(3) peritonitis; (4) destruction of large amount of hepatic tissue; (5) complications of various kinds other than peritonitis.

It is impossible to get any accurate information as to the relative frequency of the different causes of a fatal termination, because the actual cause of death is so rarely mentioned; but, so far as I can learn, exhaustion is the most serious source of danger, and a slow septicæmia—which, indeed, ultimately causes exhaustion—is next in frequency. Whatever may be the relative frequency of these different causes of death, however, one thing is quite certain: that, as a general rule, to which there are few exceptions, the longer the abscess remains without a free opening, so that its contents can be easily discharged, the greater is the danger.

The *duration* of the fatal cases was from a few days to six months—the majority died in from six weeks to three months.

The following table will show the mortality of abscesses from various causes; it will be observed that I do not include all the 110 cases in the table; those which are omitted were due to various causes, such as gastric and duodenal ulcer, peri-uterine inflammation, etc., but the cases attributable to any one cause are so few in number that no deductions can be drawn from them:

		Fatal cases.	Mortality, per. ct.
Whole number of cases	110	67	60
Cases due to dysentery	31	20	62
Cases due to injury	12	10	83
Cases due to gall-stones	8	8	100
Causes unknown	38	17	45

The other circumstances influencing the prognosis of hepatic abscess have already been considered as fully as time will permit.

The *treatment* sanctioned by results is so distinctly surgical in character that only a brief outline of it will be given here. It is scarcely necessary to mention temperance in matters of diet and drink, a pure water-supply, and probably, also, the aseptic management of wounds, as prophylactic measures. I shall not consider the influence of the treatment of dysentery on the occurrence of hepatic abscess, because it has already been considered in the papers on dysentery. It is very questionable whether any drugs are useful in cases of hepatic abscess, except in so far as they relieve symptoms and aid in the maintenance of the patient's strength.

In view of the extreme difficulty, or, indeed, the impossibility, of

determining in a given case whether there is but one abscess or more than one, and in view, further, of the results of operative treatment as compared with expectancy, surgical measures would seem to be indicated in all cases as soon as it is certain that pus has formed, unless the abscess has opened in such a situation that it can discharge freely, and unless the absence of fever and a general improvement in the patient's condition give reasonable ground for hope that danger has passed. In cases of multiple small abscesses surgical treatment would do no good, but it would as certainly, I think, do no harm; and as it is impossible, as just stated, to recognize the existence of multiple small abscesses by any special symptoms, it seems to me the patient should have the benefit of the doubt, and an attempt at least should be made to find the pus with the aspirator. Of course, extreme exhaustion would contra-indicate operation here, as in other surgical cases.

The last point to be considered, then, is the different operative measures which have been proposed and their relative value. The methods which have been proposed and practised are:

1. Aspiration alone.
2. Aspiration and subsequent washing out of the cavity with some antiseptic solution through the aspirator-needle.
3. The use of a large trocar and canula alone.
4. The use of a large trocar and canula, the canula being subsequently left in to secure drainage.
5. Incision.
6. Incision and drainage.
7. Incision and washing out with some antiseptic solution, with or without subsequent drainage.

Practically, these seven may be reduced to three, namely:

1. Aspiration.
2. Incision and drainage.
3. The use of antiseptic washes.

I shall have nothing to say as to the use of Vienna paste before the incision to insure adhesion between the liver and abdominal walls, or of the use of acupuncture for the same purpose, or of stitching of the liver to the walls, etc. These are distinctly surgical measures, and do not properly belong in this paper.

Aspiration was practised in 17 of the cases which I have analyzed.

Of these 17 cases, 7 ended in recovery, and 10 were fatal. In 4 cases, however, aspiration was followed later on by free incision and drainage, and of these 4, 3 recovered and 1 died. In one of the recoveries, after aspiration the cavity was washed out with carbolic solution through the aspirator-needle.[1]

Incision and drainage was practised in 48 cases, and of these 35 ended in recovery, and 13 were fatal. Of the 35 cases which ended in recovery, antiseptic injections were used in 12; and of the 13 cases which ended fatally, antiseptic injections were used in 2. Of the 35 cases which ended in recovery the abscess was attributed to dysentery in 10 cases; to injury in 2, to an ulcer on the leg in 1, and in 22 cases the cause was unknown. The causes of death were as follows: in 5, the presence of other abscesses; in one of these there was an abscess in the brain also; in another the abscess which was incised had healed. In the cases of single abscess death resulted from exhaustion three times, from peritonitis once, from pneumonia once, from waxy degeneration of the liver and kidneys once, and from persistent diarrhœa once. In only one case, that of peritonitis, could the result have been due to the operation.

The value of prompt incision and drainage is perhaps universally recognized now, but I trust the statistics which I have given, dry as they are, may not be without value. I would refer again, in conclusion, to the statistics on this point of Ferron, to which I have previously alluded. In 47 cases of antiseptic hepatotomy for hepatic abscess which he collected, there were 10 deaths which were caused as follows: 5 were due to multiple abscesses, 1 to pulmonary trouble, 3 to complications, and 1 to peritonitis, brought on by a counter-opening fifteen days after operation. In 39 cases of single abscess, he says death followed antiseptic hepatotomy only once. Of the 8 cases of multiple abscesses, 5 terminated fatally. Of the 13 fatal cases there was but one abscess in 7; there were more than one in 5, and in 1 the number is not stated.

The following conclusions, it seems to me, are either warranted or rendered highly probable:

1. That hepatic abscesses rarely occur as a result of injuries or

[1] Aspiration is *very rarely* dangerous, but it is not absolutely free from danger. Dr. J. C. Reeve, of Dayton, Ohio, has reported a case in which death occurred as the needle was being introduced, and Dr. Godlee refers to the danger of internal hemorrhage from the needle puncture.

diseases of the bones or other parts of the body, except those directly connected with the portal system of veins, or immediately adjacent to the liver.

2. Ulceration of the bowels is a common cause of hepatic abscess, but neither the morbid changes nor the symptoms are those of simple dysentery. It is probable that in most cases, at least when the hepatic abscess is due to dysentery, the latter disease is amœbic in character.

3. An hepatic abscess may appear in two weeks from the commencement of the dysenteric attack, but the usual time is from four to twelve weeks. It is impossible to say how long a time must elapse after an attack of dysentery before all danger of hepatic abscess is past.

4. Abscesses originating in the bile-ducts and those due to injuries of the liver itself seem to be of comparatively rare occurrence. When due to injury, the abscess usually appears in a few days.

5. Abscesses occurring in connection with general septicæmia or pyæmia are probably nearly always multiple in number and small in size, but in rather more than half of all other cases the abscess is single and comparatively large. Abscesses due to gall-stones, however, are usually multiple.

6. Aspiration occasionally fails to reveal an hepatic abscess, because the needle may not enter it, or the contents of the abscess may be too thick to flow through the needle.

7. There are no means of determining with certainty the presence or absence of adhesions in a given case; pain, tenderness, and œdema over the seat of the liver suggest the presence of adhesions, but are by no means certain proof of their existence. Even the up-and-down movement during respiration of a needle inserted into the liver is not a conclusive proof that adhesions do not exist, as was shown by a case recently under my care.

8. Of the symptoms and signs of hepatic abscess, pain, tenderness, and swelling in the hepatic region are by far the most important. Fever is present in a large proportion of cases, is intermittent in character, and except in pyæmic cases rarely rises above 102.5° or 103°. Jaundice and ascites nearly always denote the presence of dense adhesions, or gall-stones. Dyspnœa and cough are frequently present.

9. It is doubtful whether absorption of the contents of an hepatic

abscess ever occurs; bursting is of frequent occurrence, the most usual direction being into a bronchus, or the pleural cavity. Under expectant treatment death occurs in a large proportion of cases before bursting.

10. With respect to treatment, free incision and drainage give far better results than any other mode. The results of aspiration are rarely satisfactory, nor is aspiration itself entirely free from danger.

A CASE PRESENTING THE SYMPTOMS OF LANDRY'S PARALYSIS, WITH RECOVERY.

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M——, a native of Baltimore, thirty-three years old, well-built, rather corpulent than muscular, temperate in all his habits, and accustomed to lead a very quiet life; had been in good health previously to the attack about to be described.

On November 26, 1891, he took cold, for which he took quinine and mustard baths. On November 28th he got wet by rain. He now experienced intermittent pain in the calf of the leg. About December 1st he observed, to use his own language, "a cold feeling across his toes, as if he had dipped them in cold water;" also the same cool feeling attacked "the left upper lip [*sic*], as if it were chapped and air blew on it." These ill feelings continued till December 6th. On that day he was about the house, as usual; but in the afternoon, on attempting to go up stairs, in his own words, "Very much to my surprise, I found I did not have the power to raise the left leg from one step to the other without serious exertion in the way of dragging it." In a few days he took to his bed, "being unable to hobble around any longer." The feeling of coolness and numbness continued to get worse, and to extend upward on his legs to the knees, and also invaded the hands and arms to the elbows, the muscular power steadily failing from the lower extremities upward.

The patient was under the care of Dr. F. Chatard, of Baltimore, who kindly asked me to see him, and to whom I am indebted for many details of the case. I first saw the patient on December 17th. His condition was then as follows: The lower limbs were completely paralyzed, but not emaciated or flabby. The muscles of the trunk and belly were greatly weakened. The man could give a wriggling motion to his hips, but could not sit up or turn on his side. He coughed, but with very little force. The hands and arms were quite weak, with a tendency to assume the position of wrist-drop. The shoulder-movements were good; the face was not affected. Sensation was apparently normal, except that the sensation of tickling on the sole of the foot was nearly or quite lost. The power of localizing correctly any point of the foot touched was retained. Farado-cutaneous sensibility was apparently normal. The man

could distinguish hot and cold objects. No pain was elicited on pressing the muscles. The reflexes, both superficial and deep, were completely lost.

Tested with the faradic current, the muscles responded, as nearly as I could judge, normally. The patient's subcutaneous layer of fat was thicker than usual. To the galvanic current the muscles responded normally, contracting quickly without a sign of degenerative reaction, with no quantitative or qualitative alteration. The muscles also contracted from nerve-stimulation. The sphincters were absolutely intact. After this, for three or four days, the paralysis increased in the upper extremities until he could no longer use his hands. The abdominal muscles became so weak that he could not cough. The facial nerves now became involved in all of their branches, more decidedly, however, on the left side. The patient could not frown, could not close the left eye, could with effort barely approximate the lids of the right so as to make them touch, and could not whistle. Articulation was somewhat defective from the weakness of labial muscles. The tongue was unaffected, except that the patient stated that it felt thick. He was restless, and said that he felt as if he was being smothered by his own weight.

The breathing became oppressed, and he had several attacks of threatened suffocation. (The action of the heart was not affected, either in frequency or force.) At this point the progress of the disease seemed to be arrested, and then improvement, especially of the respiratory symptoms, began and proceeded somewhat rapidly, the face and arm recovering first. On the first of January, 1892, he could raise himself in bed; on the 7th he sat up on the side of the bed; on the next day he dressed himself; on the 13th he was able to walk alone; and on the 20th he was able to leave the house. I saw him about a month later. His limbs were not thinner than natural, though still a little weak. The patellar reflex was still absent.

This case seems to me worthy of record, because of the very close resemblance of its symptoms to those of Landry's paralysis. Indeed, I do not see why it should not be considered as a case of that disease. It is noticeable that the symptom of oppression and difficulty in breathing that usually closes the scene in fatal cases of Landry's paralysis, was prominent, and appeared to lack but little of severity sufficient to have caused death.

Dr. Cramer, in the January number of the *Centralblatt f. Pathologie u. pathologische Anatomie*, after having given an admirable analysis of the best-studied cases of Landry's paralysis, concludes that "with the symptom-complex that we call Landry's paralysis, the peripheral nerves alone, as well as the central nervous system with the peripheral nerves, may be diseased" (the peripheral nerves being in almost every case affected); and, moreover, "that the origin of the disease is to be found in the toxic influences of invading microörgan-

isms." From this standpoint there seems to me but little difficulty in supposing cases of varying severity and termination according as the central nervous system (the respiratory and cardiac centres) or the nerves of respiration are more or less deeply affected by the toxic agent. One point seems to be impressed by this case—namely, the difficulty, or rather impossibility, in certain cases of differentiating between the peripheral and central (spinal) origin of symptoms, especially of paralysis. I think we should keep more in mind that the whole motor system—peripheral nerves, nerve-cells, and central tracts—is so much of a unit, that while the insults of disease may confine themselves to one segment of the apparatus, we may reasonably expect disease of one part to extend to others or all.

A CASE SHOWING SYMPTOMS OF LANDRY'S PARALYSIS; RECOVERING.

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In all diseases whose pathology is imperfectly understood great changes are liable to take place from time to time as to our conceptions of them. This is emphatically the case with Landry's paralysis. Since it was first prominently brought to the notice of the profession by Landry, in 1859, almost every variety of rapidly spreading paralysis has been described as belonging to it.

The opportunity of observing cases occurs so rarely, even to those of widest experience, and death usually results so rapidly after the onset of the symptoms—too rapidly apparently for definite morbid lesions to be developed—that there appears little prospect of an early settlement of the pathology. The cases ending in recovery have been so various in their symptomatology that they, too, have added little to our knowledge of the disease.

The following case, which I had the privilege of seeing on several occasions with my friend, Dr. N. A. Powell, of Toronto, and to whose kindness I am indebted for the notes of it, presents in a striking manner the phenomena of Landry's paralysis.

G. E. W., a clerk, aged twenty-six years. With the exception of malarial fever fifteen years ago, has always been healthy.

His present illness began December 2, 1891. For three or four days before this he noticed some uncomfortable sensations in the feet, which he supposed due to his boots. During last summer he had excessive perspiration of the feet; never had such perspiration before. On the morning of December 2d, after stooping to open the safe, he found it difficult to rise again to the erect position; had to use his arms to assist himself to rise. The weakness of the legs increased during the day so that he had much difficulty in ascending

stairs. In the evening he found great difficulty in putting on his overcoat; this was the first sign of weakness in the upper extremities. Next morning, on rising, the legs were very weak; was able to dress and walk down stairs, but had immediately to lie down on a sofa. Weakness of the hands rendered dressing troublesome; some muscular pains in forearms and shoulders.

December 4th. Paralysis of all the extremities complete; those of trunk and neck also involved, so that the head could not be raised from the pillow. Speech, swallowing, and breathing unaffected; sensation normal; bladder and rectum acted normally, but no straining could be exerted to evacuate their contents; knee-jerk absent. Electrical reaction normal.

10th. No change noted in symptoms until to-day, when speech became somewhat thick.

12th. Swallowing slightly affected, so that there was considerable difficulty in taking soft food. This difficulty soon improved and disappeared in a few days, as did also the difficulty in speaking. Breathing normal, and remained unaffected.

13th. Some pain in lumbar region; relieved by heat. It recurred frequently for a week.

20th. Reflexes still absent; no wasting; no tendency to bedsores; able to move the hands and forearms slightly.

January 1st. Power of motion had returned in all the extremities to a slight degree, being most advanced in the upper. He is able to maintain the sitting posture in an arm-chair, and can hold the head erect for a few seconds without support. Knee-jerk quite distinct in right, and very slight in left knee.

February 3d. Able to walk a few steps unsupported; uses his hands freely, though the muscular power is still very poor.

He continued to improve and was soon able to walk fairly well; knee-jerk became somewhat exaggerated; no ankle-clonus. Sitting with his elbows resting on the arms of his chair and hands extended; marked tremor of forearms and hands occurred while the position was maintained.

April 20th. Looks vigorous and walks well, but if he allows the knees to bend much they give way under him; knee-jerk slightly increased. Electrical reaction continued normal throughout. The spleen could not be felt at any time, although the area of dulness was slightly increased.

May 22d. Has continued to improve steadily; able to walk for two or three hours. Upper extremities, especially above the elbows, proportionally stronger than the lower. He is just able, when standing, to raise himself on the front part of the foot.

There appears to be slight wasting of the interossei muscles of the hands; but these as well as all the other muscles of the hands react to faradism, but they require a strong current. To galvanism the response is also more difficult to elicit, but it is quite normal in each of the muscles. There is no wasting apparent in the feet, and electrical reaction is normal, though requiring a comparatively strong current. Plantar reflex is present, but feeble, as is also the cremasteric; epigastric reflex cannot be obtained.

Such, briefly, is the history of this case. It presents very completely the symptom-complex of Landry's paralysis. The only departure from the descriptions of that disease is the absence of disturbance of respiration—a symptom so frequently present in these cases. This is the more remarkable, in view of the disturbance of both speech and deglutition.

The symptoms, as a whole, indicate the spinal cord as the seat of lesion. The absence of trophic and sensory disturbances, the preservation of normal electrical reactions, and the knee-jerk go to prove the integrity of the nerves and their roots and the absence of any material lesion of the ganglionic cells of the gray matter of the cord.

As to the causation of the disease, the most generally accepted opinion points to a toxic agent resulting from an invasion of micro-organisms—not necessarily of the blood, but more often of some local part, with subsequent absorption of their toxic products into the blood. In this way the disease has been found to follow many of the acute fevers. There is no history of acute disease in this case, but at the time the patient became ill an epidemic of influenza was beginning. Two other cases are now under observation in the Toronto General Hospital whose symptoms closely resemble those of Landry's paralysis, and in both these the illness began during the same epidemic; in neither is there any history of illness preceding the paralytic attack. In the epidemic of 1890 Bernhardt[1] had two cases presenting the symptoms of Landry's paralysis; in one slight bronchial catarrh occurred two weeks before the attack, in the other a slight cough preceded the onset of the paralysis for a day or two only.

Microörganisms of various kinds have been found in cases of supposed Landry's paralysis, such as the bacillus of anthrax;[2] the bacillus of typhoid;[3] staphylococci,[4] and other microörganisms. In other cases most carefully examined, however, no germs could be found in connection with the nervous system, although in some infective processes existed in other parts. That the cause is toxic, in some cases at least, is rendered practically certain by such post-mortem evidences of blood infection as tumefied spleen, hemorrhagic foci in the lungs and intestines, swollen mesenteric glands, etc. In

[1] Wien. klin. Wochenschrift, 1890, No. 40.
[2] Deutsche med. Wochenschrift, 1890, No. 38. [3] Ibid. [4] Ibid.

some cases, however, there is no evidence of acute disease, nor was any epidemic prevalent at the time of attack.

As already stated, on the pathology the most divergent views continue to be held by different observers. Some, especially German observers, include all cases showing the symptom-complex of the disease, whether depending on lesions of the spinal cord, or of the nerves, or of both. In fact, the majority seem to believe that the peripheral nerves suffer in almost all cases, in some with only slight lesion of the cord. Most English and American writers, on the other hand, restrict the term to cases showing signs of lesions of the spinal cord only, and classify those with lesions of the nerves as multiple neuritis.[1]

The results of the post-mortem examinations in the reported cases are of the most varying character.[2] The earlier reports consist chiefly of the negative results obtained from examination of the central nervous system. Of those lately reported, Nauwerck and Barth[3] found advanced interstitial neuritis in the nerves of the cauda equina, as well as of the anterior roots of all the spinal nerves. Centanni[4] found a peripheral neuritis with slight affection of the spinal cord. In most of the affected parts, especially in the endo-neural lymph-spaces, there were many microörganisms which he believed to be the active agents in the causation of the disease. Eisenlohr[5] reports two cases in both of which the peripheral nerves were affected, and the spinal cord in one. Last year Hun[6] gave the clinical history and post-mortem results in a case in which only a little recent inflammation of both cerebral and spinal meninges, and slight degeneration of some fibres of cauda, were found, but the condition of the nerves is not stated.

The latest, and perhaps most interesting, contribution to this subject was made by Klebs[7] last year. In his case the peripheral nerves, on careful examination, revealed no change; but in the spinal cord hyaline thrombosis was found throughout the central artery of the cord and of its branches extending into the cord as far as the anterior

[1] Osler: Practice of Medicine, 1892, p. 835.
[2] Centralbl. f. allg. Path. u. path. Anat., Jan. 1, 1892.
[3] Ziegler's Beiträge, 1889, Band v.
[4] Ziegler's Beiträge, 1890, Band viii.
[5] Deutsche med. Wochenschrift, 1890, No. 38.
[6] Hun: Boston Med. and Surg. Journ., vol. cxxiv. p. 485.
[7] Deutsche med. Wochenschrift, 1891, No. 3.

cornua. There were also some small hemorrhages in the region of the thrombosed vessels and some exudate about the ganglionic cells of the anterior cornua.

He describes very fully the arterial supply of the cord. The cornua receive branches from the central spinal artery, which is reinforced at each intervertebral notch as it passes down the anterior fissure, by branches from the vertebral, intercostal, and lumbar arteries. Its branches of distribution penetrate the cord from the anterior median fissure. The branches from the vertebral, intercostal and lumbar arteries, as they enter to join the central artery, themselves give off branches which penetrate the cord directly at the anterior roots and anastomose with the branches of the central spinal artery, so that the inter-ganglionic capillary plexus receives its supply from both sources, the latter being in much more direct relationship to the aorta. The hyaline thrombosis, which Klebs found, was confined to the central spinal artery and its branches extending into their capillaries in the anterior cornua. In consequence of this the whole supply of blood to the anterior gray matter would be derived from the more direct arterial source; the disturbance would result in increased and irregular vascular pressure in this area with consequent hemorrhage and a varying degree of serous and cellular effusion. Klebs ascribed the symptoms in this case directly to these vascular changes and the nutritive disturbances depending thereon. He believed also that the thrombosis was not of vascular origin, but due to enzymes formed by microörganisms, which, in this case, were probably tubercle bacilli, as there was found at the autopsy a fresh tubercular pericarditis caused by perforation of the pericardium by a caseous bronchial gland. He believed, moreover, that the cord must be the essential seat of the lesion in all cases, and that any affection of the nerves should be viewed as a complication. He freely confessed, however, that for the proof of such views we must have recourse to experimental research.

I have thus fully epitomized Klebs's views, because the conditions described so fully account for the symptoms and indicate with certainty the seat of lesion, at least in some, a part that should be most carefully examined in all future cases.

It would seem wiser, with Klebs, to view the peripheral nerve-lesions as complications, than, with the majority of English and

American authors, to look upon them as multiple neuritis distinct from Landry's paralysis, thus classifying them as a separate disease although produced by the same causes and occurring under similar circumstances.

Such hyaline thrombosis, however, cannot be present in all cases, as equally capable observers have found these vessels normal in cases that were quite as typical. It would seem that not only the seat, but also the nature of the morbid change may vary; and that the cause also may be different in different cases. The chemical products of a great variety of germs seem capable of producing the disease. In some of the rapidly fatal cases it may be that these poisons expend their force on the terminal plexus in which the pyramidal fibres of the upper segment of the nervous system terminates in the gray matter of the cord, as suggested by Gowers,[1] inhibiting or interrupting the connection between the anterior cornua and the psycho-motor zone of the brain, and causing death by paralysis of the respiratory function, before lesions tangible to even present methods of investigation are produced; while in the more slowly progressive cases, the poison exerts its influence on some other part of the spinal cord, on the nerve-roots, on the nerves themselves, or on all these parts simultaneously, producing the varying results found on post-mortem examination.

That such widespread nervous phenomena lasting even only a few days can be produced by a toxæmia, of whatsoever source, without causing any morbid changes in the parts implicated, seems scarcely credible. That some pathological changes must be produced, at least in the recovered cases, is placed beyond doubt by the persistence of the symptoms and the tedious convalescence; no agent simply disturbing the function of a part, however slightly, could maintain its influence for months without injury to the histological elements. The action of morphine, strychnine, etc., has been cited to illustrate the probable mode of action of a chemical bacterial product in this disease, but the action of such poisons is relatively very evanescent; as soon as their excretion is completed the affected parts promptly regain their wonted vitality, and the sufferer is restored to his normal condition. Should the disease prove to be due to toxic agents acting

[1] Diseases of the Nervous System, 2d ed., vol. i. p. 384.

on the nervous system, producing symptoms of rapidly ascending paralysis, it would seem not only more rational, but also more conducive to a broad conception of the disease and its pathology, to include in the category all the aspects of the disease, whether affecting the spinal cord, or the nerves, or both. If thought desirable, the cases might be further classified, according as the cord, or nerves, are most seriously affected, rather than designating the same affection of these different parts as different diseases.

A case of recovery, no matter how carefully observed, does not furnish sufficient grounds on which to offer any theory of the pathology of the disease. My object has been to bring to the notice of this Association a case presenting in a striking manner the symptom-complex of this rare affection of the nervous system, with a brief reference to the recent literature on the subject, and to point out the desirability of considering all cases showing the distinctive symptoms as examples of the disease, whether the seat of lesion be found in the cord or nerves.

DISCUSSION.

Dr. Charles Cary: I would like to report a case which came under my care a year ago, presenting the same line of symptoms, but differing in one or two points from the cases recited.

A woman, aged forty-eight years, the mother of a family, had enjoyed previous good health; was addicted to either morphine or chloral or some other allied habit for many years, and came under my care for relief from that trouble. She was in the habit of getting up once or twice a day and taking sulphonal. At the end of five or six days her store of sulphonal became exhausted, and she began to complain of difficulty of locomotion. She had been a general complainer, and so I did not observe her symptoms very closely. When she had been under my care about a week I observed a marked paralysis of the lower extremities below the knee. This paralysis crept up, gradually involving first the entire lower extremities, then both vesical and rectal sphincters. Later, the abdominal muscles. Coughing became impossible; efforts at vomiting were imperfect; finally there was complete and absolute paralysis of the upper extremities and a great deal of respiratory difficulty; she complained of a sense of suffocation which at one time became very threatening; her pulse became frequent, reaching gradually 130 beats per minute, which makes this case differ somewhat from the others presented. When her respiration became involved and she had these

attacks of suffocation, her pulse became hardly perceptible. Deglutition was difficult, and articulation was lost. She was able to whisper, but there was no phonation, and her articulation was very imperfect. For about two days I had no expectation of the woman's recovery. Although there was no loss of sensation there was complete paralysis. From that she began to make gradual recovery by beginning, in the first place, to speak a little more perfectly and then to move her extremities by creeping her fingers along on her body to where she wanted to place her hand. Finally the thoracic muscles became restored in a measure, and so on down the entire body. Now she is apparently in as good health as before the attack. Perhaps one of the reasons why the anal sphincter appeared to be paralyzed was because I was obliged to give her cathartics. I cannot, however, explain about the vesical sphincter.

The case was seen by other physicians: by Dr. Stockton, a member of this Association; Dr. Andrews, Superintendent of the State Insane Asylum at Buffalo; Dr. Hurd and others; and so far as the aggregate of symptoms was concerned, we were of one accord that it was a case of so-called Landry's paralysis, or acute ascending paralysis. The case has not yet been reported.

Dr. W. H. Thomson: It seems to me that the involvement of the sphincters rather excludes this case from Landry's paralysis. I have had one typical case in which the usual course of rapidly developing ascending symptoms, ending in death, occurred, and in which nothing in the shape of peripheral neuritis was found nor any centric lesions, by Prof. Delafield, who made the post-mortem.

The second case, now in Bellevue Hospital, is one of some doubt in my mind. His history is interesting. The attack came on, he said, with loss of power in the left leg; very soon the right leg was involved; then he was paralyzed in the lower part of his body, but never had any trouble with micturition, or with his bowels; then he said that his arms became paralyzed; then occurred difficult respiration, but no symptom whatever connected with the hypoglossal; no bulbar symptoms, except one—he had entire paralysis of the lower jaw. This would indicate that the process stopped short of involving the other bulbar centres; his jaw remained paralyzed for over two weeks, and he was obliged to be fed. These symptoms all passed off except some weakness in mastication and moderate weakness in the upper extremities, the right being more affected; but permanent weakness remained in the lower extremities. His gait is neither ataxic nor paraplegic. It is now eleven months since the attack. The paralysis took nine days to develop, although, having to depend entirely upon the patient's statement, there may be some doubt about the details. He has no loss whatever of electrical excitability; he shows no signs of atrophy of any muscle; never had any sensory symptoms whatever.

Dr. Miles: Deglutition was slightly affected in my case.

LOCAL ANÆSTHESIA AS A GUIDE IN THE DIAGNOSIS OF LESIONS OF THE LOWER SPINAL CORD.

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Every fact which bears upon the exact localization of disease in the nervous system is entitled to most careful study, for the experience of the past ten years has demonstrated that the surgical treatment of nervous diseases—a treatment more radical, and sometimes attended by far greater success than medical treatment—must rest upon accurate diagnosis.

The study of motor disturbances, both of the form of paralysis and of the form of variations in reflex activity, has made it possible to determine the situation of lesions in the spinal cord with some exactness. The level of the cord at which the various reflex acts are performed is quite well known. The extent through various segments of the cord of those groups of cells which govern various muscles is also settled.[1] But the spinal cord has sensory as well as motor functions, and it is only within a short time that the disturbances in sensation occurring in spinal lesions have been utilized for purposes of diagnosis.

This is partly due to the fact that the examination of sensory defects is tedious, and the results may be quite uncertain unless great care is taken in mapping out upon a convenient diagram the areas of anæsthesia. It may be partly due to the fact that the method of examination is often imperfect. For in examining for sensory defects it is always to be remembered that the test involves a contrast

[1] See "Syringomyelia," The American Journal of the Medical Sciences, May, 1888.

between two sensations, a process of comparison in the mind of one perception with another, and unless the two perceptions are presented simultaneously, such comparison is apt to be imperfect. It is not enough to ask a patient whether he feels the touch of the cotton-wool, or the tip of the finger, or the warm or cold test-tube, or the prick of the needle, or the sting of a faradic brush; nor is it sufficient to touch two parts successively, and demand that he compare a sensation with a memory. He should always be tested upon two surfaces simultaneously, and asked if any difference is felt between the sensations. The necessity of this is evident when it is considered, yet observation has convinced me that it is not the method commonly employed. In spinal affections we always have the face as a convenient surface with which to make comparisons; and in the diseases of the lower region of the cord, to which attention is directed in this paper, we have the arms and trunk as a standard of normal feeling.

It has been my good fortune during the past few years to observe a number of patients suffering from disease in or about the lower half of the spinal cord, who have presented very interesting disturbances of sensation. In the medical journals and works I have found a few cases of more or less similar character—some of them with post-mortem records. I hope to show from their study that a limited area of anæsthesia is produced by a limited lesion in the spinal cord; that as the lesion ascends the cord from its lowest limit upward the area of anæsthesia extends in a definite manner upon the surface of the body; and that the situation and shape of the area of anæsthesia are positive indications of the level of the lesion in the spinal cord.

These facts are not wholly new. It has long been known that in transverse dorsal myelitis the band of anæsthesia about the body corresponded to the level of the lesion. But there are many cases of myelitis of the cervical and lumbar regions of the cord in which the exact distribution of anæsthesia has been overlooked. This is especially true of lumbar and sacral myelitis, which is the form most frequently met with, and which alone will be considered in this paper. The situation of the anæsthesia in lesion of the lower part of the cord is such as to escape attention unless searched for; and as the patients lie in bed upon their backs, and sensation is often preserved in the front of the legs and thighs, the examiner, being con-

tent with the investigation of these parts, is misled into supposing that there is no anæsthesia.

The exact area of anæsthesia in lumbo-sacral myelitis has been investigated by various clinical observers, and isolated cases have been recorded.[1] Thus Westphal, Rosenthal, Huber, Bernhardt, Oppenheim, and Eulenberg, in Germany, Ross and Thorburn, in England, and Osler, Mills, Herter, and Church, in this country, have recorded cases. French observers who have made careful study of hysterical anæsthesia have appeared to overlook this subject. The only effort to bring the recorded cases together and make deductions from them has been made by Thorburn in his work upon the *Surgery of the Spinal Cord*. Since that work was written several important cases have been published with autopsies. As I have had the opportunity of seeing six cases in which limited areas of anæsthesia aided the localization of the lesion, it has seemed proper to record these cases and review the subject carefully. The cases of special importance will first be described, and the conclusions from their study will then be considered.

Case I. (Starr.) *Injury; sphincteric paralysis; limited anæsthesia; lower sacral lesion.*—The first case is that of an engineer, J. L., who met with an injury in July, 1891, his engine falling some thirty feet, while he remained in a sitting posture in it, and thus received the blow upon his lumbar region, where there still remains the evidence of injury in a slight protrusion of the first and second lumbar spinous processes, with some induration about them. He found himself unable to rise after the fall, felt much pain in the lower sacral region and at the upper lumbar vertebræ, and at once lost control of his bladder and rectum. For five weeks after the injury he lay in his bed, though able to move his legs freely; and after this he got up and has walked, and now (March, 1892) walks perfectly well. The only evidence at any time of motor trouble was a twitching of the muscles of the outer side of the legs below the knees, which persisted for several months after the injury, but has now passed away. According to his statement, this twitching must have been limited to the peronei in both legs. For four months after the injury he was obliged to use a catheter and to wash out his rectum. At present

[1] Westphal: Charité Annalen, 1882, i. 421. Rosenthal: Wiener med. Presse, 1887, xxix, 670. Huber: Wiener med. Wochenschr., 1888, xxxviii. 1310. Bernhardt: Berl. klin. Wochenschr., 1888, xxv. 637. Oppenheim: Arch. f. Psych., 1889, xx. 298. Eulenberg: Zeitschr. f. klin. Med., 1890, xviii. 547. Ross: Brain, 1887, x. 333. Thorburn: Brain, 1887, x. 381. Osler: Medical News, December 15, 1888. Mills: Medical News. March 1, 1890. Herter: New York Medical Journal, August 22, 1891. Church: The American Journal of the Medical Sciences, April, 1892.

(March, 1892) his sphincters are not under perfect control, his urine flowing as soon as his bladder is moderately full, though it never dribbles away, and his rectum occasionally emptying itself suddenly. He is however, slowly regaining control of both organs, but there is little resistance at the anus, and he wears a napkin.

From the day of the accident to the present time he has felt a numb sensation in the lower sacral region, in the perineum, and back of the scrotum in the area shown in the diagram (Fig. 1). He is an intelligent man, and is quite certain that the sensory disturbances in this area have not varied, having been tested by several physicians since the injury. An examination shows a total loss of temperature- and pain-senses in the area marked out, and a marked diminution, but no loss, of tactile sense. The diminished tactile sense extends over the entire scrotum and posterior half of the penis, and is possibly the reason for an imperfect power of connection of which he complains, his sensations being slight, the flow of semen premature, and erection too short in duration, although he has impregnated his wife since the accident. There is no trace of anæsthesia of any kind elsewhere in his body. His knee-jerks are normal. The gluteal reflexes are absent. No ankle clonus. The complete absence of any symptoms of traumatic neurosis is interesting, and also the gradual improvement in the motor, reflex, and automatic symptoms, the only permanent symptom being the total anæsthesia to temperature and pain and the partial anæsthesia to touch in the limited area.

The diagnosis was a hemorrhage in the lowest part of the spinal cord.

Case II. (Rosenthal.) *Sphincteric paralysis; limited anæsthesia; sacral lesion.*—Female, aged thirty-six years. After exposure to cold and fatigue, felt some pain in urinating and numbness in her buttocks. Four days later the pain and numbness had increased, she began to have retention of urine, and lost control of her rectum. Seven months later, when seen by Rosenthal, she was found to have anæsthesia to all sensation in the area shown in Fig. 2, including the genitals up to the mons veneris; she had no control of the bladder, which emptied itself spontaneously every two hours; she had no control of the rectum, and could move the bowels by enema only—but was perfectly able to walk. This condition had persisted for four years when the case was reported.—*Wiener med. Presse*, xxix. 670.

Rosenthal ascribed the condition to a hemorrhage, with destruction of the lowest part of the spinal cord.

Case III. (Westphal.) *Sphincteric paralysis; limited anæsthesia. Autopsy—gumma of cauda equina.*—Female, aged thirty-six years; began to suffer in September, 1874, from pain in the legs and fatigue on exertion, with some numbness from the feet to the knees and a disagreeable sensation of pressure in the rectum. Soon afterward she lost control of the rectum, and began to have retention of urine. Then anæsthesia developed in the genitals, peri-

neum, anus, and buttocks. When examined by Westphal, in December, 1874, she was found to be completely anæsthetic to touch, temperature, pain, and electricity in the area shown in Fig. 3, and also in the perineum, vagina, and over the external genitals up to the mons; there was a large bedsore in the anæsthetic area over the sacrum; there was retention of urine, which had to be drawn by catheter, the passage of which she did not feel; there was

Fig. 1. Fig. 2. Fig. 3.

Starr.

Rosenthal.

Westphal.

inability to empty the rectum, except by mechanical means; the anal sphincter was not relaxed, but grasped the finger. Motion was in no way impaired. She died December 27th, and the autopsy showed caries of the sacrum, and a gummy mass with hemorrhagic exudation and connective tissue filling the entire spinal cavity within the sacrum as high as the first sacral nerve, and compressing slightly all the sacral nerves except the first. The spinal cord was normal.—*Charité Annalen*, i. 421.

The following case, reported by Kirchkoff (*Arch. f. Psych.*, x.), is of interest, since it includes a record of post-mortem appearances.

Case IV. (Kirchkoff.) *Injury; sphincteric paralysis. Autopsy—compression of sacral cord.*—The patient, a man aged thirty years, fell from his horse upon his nates, and felt immediately severe pain in his sacral region, and was unable to rise. For three months he was confined to bed, suffering from pain in the back and retention of urine, which was followed by incontinence of urine and feces; then he was able to go about, though he walked slowly with legs rather separated. Sensation is said to have been retained when he was

examined, one and a half years after the injury. He gradually recovered entirely, except for the incontinence of urine and feces, which remained till his death, one and a half years after the injury. The autopsy showed that a portion of the body of the first lumbar vertebra had been fractured and was compressing the lowest part of the spinal cord, involving the fifth, fourth, and third sacral segments without compressing the cauda equina, the nerves of which were found normal on microscopic examination.

It is not at all impossible that there may have been a limited area of anæsthesia in this case about the perineum which escaped notice, especially if, as in my first case, the sensations of pain and temperature were the only ones permanently lost. Lachmann, however, has recorded (*Arch. f. Psych.*, xiii. 50) a case of tumor of the conus medullaris and filum terminale in which loss of sphincter control was present without any anæsthesia.

Case V. (Starr.) *Spontaneous hemorrhage into the sacral cord ; sphincteric paralysis; limited anæsthesia.*—My second case is that of a woman, R. K., aged twenty-eight years, who was seen with Dr. F. J. Quinlan in October, 1889, and in February, 1890, and whose condition since the last date has been stationary. She was perfectly well until May, 1889, when, after a day of fatigue, she was suddenly seized with severe pain in the sacral region and in the back of both thighs, with retention of urine and feces, and a sensation of numbness over the lower sacral region, in the perineum and vagina. She did not lose her power, and has been always perfectly able to walk. When examined in October, 1889, she was suffering much from pain in the lower part of the sacrum and along the back of the left thigh in the area shown on the diagram (Fig. 4). She had total anæsthesia to touch, temperature, and pain over the area shown, and this included the perineum and anus, and the entire genitalia, excepting the upper part of the labia outside the vulva. Her urine had to be drawn by catheter; her bowels were moved with great difficulty and with much pain. The sphincter ani contracted on the finger. Her knee-jerks were exaggerated. Plantar and gluteal reflexes were normal. There was no tendency to bedsores, no tenderness of the back to pressure or to heat, no girdle sensation, and no anæsthesia of the legs or thighs.

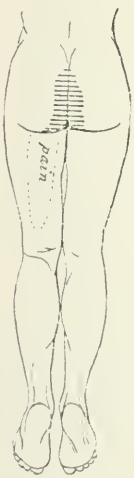
When examined again in February, 1890, she was still perfectly able to walk, but after long standing felt weak in the left leg, and found herself tired more easily than formerly. The leg was not at all atrophied, nor were the muscles paralyzed, but the response to faradism was diminished in the peroneal muscle as 60 to 45. Her bladder and rectum were still beyond her control, and were emptied by catheter and injections. She still had some pain in the back and in the left leg constantly, but recently had suffered more from pain in left ilio-inguinal region. There was no girdle sensation, spinal tenderness or bedsore. The area of total anæsthesia had increased,

and now involved the area shown in Fig. 5. A slight degree of impairment of tactile sense was also found on the outer side of the left leg below the knee, and this could be traced from the anæsthetic region downward along a narrow space on the back of the thigh, indicated by the lighter shading in the figure. The original area of anæsthesia has therefore extended. The extension has been into the former area of pain, and the present area of pain has shifted from the back of the left thigh to the left groin.

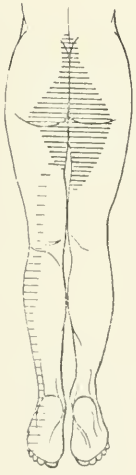
It is also of interest to find that as the lesion has advanced upward and at last begun to invade the motor part of the spinal cord, it is in the peronei that the first sign of weakness—the diminution of the faradic contractility—has begun, thus confirming the statement of Leyden that these muscles are controlled by the lowest group of cells in the spinal cord (*Klinik der Ruckenmarkskr.*, i. 41).

Here, again, as in the first case, it is to be noticed that the areas of tactile disturbance and temperature and pain disturbance do not

Fig. 4. Fig. 5. Fig. 6.



Starr.



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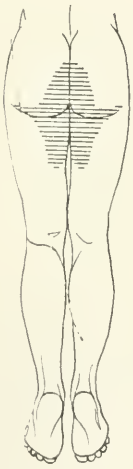


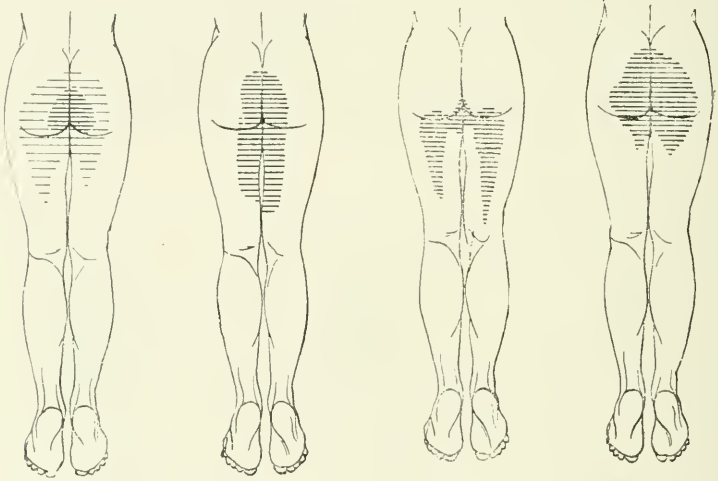
Oppenheim.

at present exactly coincide, and this seems to support the original diagnosis of a hemorrhage into the conus medullaris and lower sacral segments of the spinal cord. Such a hemorrhage might set up a chronic meningo-myelitis, and as this advanced slowly upward the symptoms would increase as they have done. Such was the

lesion in the following case of Oppenheim, which is reported with autopsy, and in which it will be noted that the final area of anæsthesia coincides quite closely with that in this case of my own.

Case VI. (Oppenheim.) *Injury; sphincteric paralysis, limited anæsthesia. Autopsy—hemorrhagic sacral myelitis.*—The patient fell upon his buttocks and immediately lost control of his legs, and felt a numbness in them. His urine was retained. He was taken to Charité Hospital, and observed there until his death, three months later. The permanent symptoms were: loss of Achillis tendon reflex, loss of control of the bladder and rectum, loss of power

Fig. 7. Fig. 8. Fig. 9. Fig. 10.



Huber. Bernhardt. Osler. Mills.

of erection, loss of sensation, especially for painful sensations in the area indicated in Fig. 6, which included "the entire vicinity of the anus, the gluteal, perineal-scrotal region and the penis, and a narrow area reaching downward on the posterior inner surface of the thighs, and upward over the lower half of the sacrum." It is to be noticed that the loss of the pain-sense was more complete than that of tactile sense.

The autopsy showed a fracture of the first lumbar vertebra and a crushing of the posterior part of the conus medullaris and disintegration of the lower two-thirds of the sacral portion of the cord. "In the lowest portion the posterior half of the spinal cord seemed entirely destroyed, as if it had been cut off by an incision through the posterior columns 1–2 mm. behind the posterior commissure. The boundary is, however, by no means a regular one, but was encroached upon by a thick, very vascular tissue full of round cells, a part of the pia mater infiltrated with granular cells, small

and large collections of blood-cells and new capillary vessels. The anterior part of the cord was also altered, being infiltrated with small round cells, while the nerve-cells were in part disintegrated. It was evidently a traumatic myelitis with hæmato-myelia." The only lesion in the lumbar enlargement was the ascending degeneration in the posterior columns. The nerve roots coming from the lowest part of the cord were involved in the lesion, being matted together in the thickened pia, but a microscopic examination showed that the nerve-roots which issued from the two upper sacral and lumbar portions of the cord were not affected, although they had to pass through the narrowed canal.—*Arch. f. Psych.*, xx. 298.

Cases almost identical in character are reported by Huber,[1] Bernhardt,[2] Osler,[3] and Mills,[4] without autopsies. The area of limited anæsthesia is shown in the accompanying figures. (Figs. 7, 8, 9, and 10.)

In the following case, reported by Herter, which was seen by me at his request, the area of anæsthesia was slightly more extensive. The case was completed by a pathological examination.

Case VII. (Herter.) *Injury; paraplegia, sphincter paralysis, limited anæsthesia. Autopsy—hemorrhage in spinal cord.* Male, aged thirty years, was crushed by a heavy weight on August 26, 1890, and immediately paralyzed in the legs and had involuntary passage of urine and feces. Five weeks later, when the effects of the shock had disappeared, the paralysis of the feet and legs remained with atrophy and reaction of degeneration below the knees, but the thighs could be moved; the bladder and rectum were totally paralyzed, neither sphincter offering any opposition to pressure; sexual power was lost; a bedsore had formed over the sacrum, and anæsthesia was present in the area shown in the diagram (Fig. 11) and included the perineum and genitals. The darker area over the buttocks was totally anæsthetic to touch, temperature, and pain; the lighter area was partially anæsthetic. The soles and dorsal surfaces of the feet were quite anæsthetic and analgesic. The patient improved during the following five months so that he was able to walk, but the anæsthesia remained the same. I saw the patient, with Drs. McCosh and Herter, in January, 1891. From the beginning there had been a prominence of the first lumbar spine, and on January 27, 1891, the operation was undertaken, and the spines and laminæ of the first, second, and third lumbar vertebræ were removed, and the cauda equina was exposed. Nothing could be found at the operation. The patient died forty eight hours later.

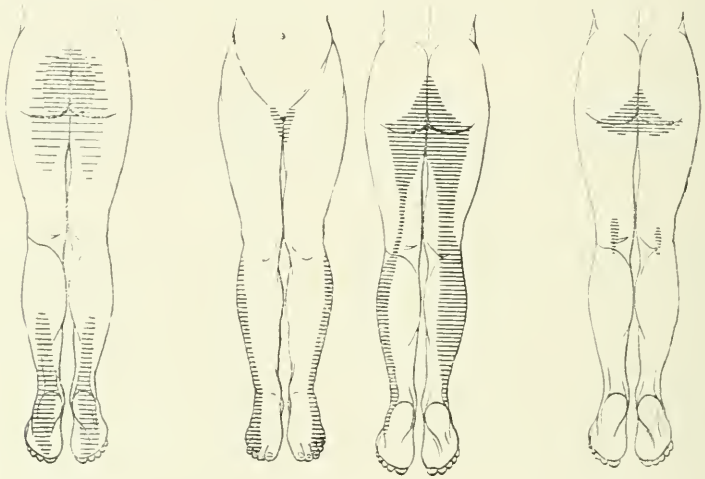
The autopsy showed the existence of an old hemorrhage and a mass of inflammatory material in the cauda equina and involving the lower three-quarters of an inch of the spinal cord. The nerve-fibres of the most centrally

[1] Wien. med. Wochenschr., 1888.
[2] Berl. klin. Wochenschr., 1888.
[3] Medical News, 1888.
[4] Ibid., 1890.

situated strands of the cauda were completely degenerated. The anterior strands also contained degenerated nerve-fibres. The lateral bundles escaped. The conus medullaris was destroyed. The lesion did not reach as high as the fourth lumbar roots, which were normal.—*N. Y. Med. Journ.*, Aug. 22, 1891.

In the following case, recorded by Eulenburg, the hemorrhage was spontaneous and not traumatic in origin, and the subsidence of the symptoms indicated a gradual absorption of the clot.

Fig. 11. Fig. 12. Fig. 13.



Herter. Eulenberg. Eulenberg.

Case VIII. (Eulenberg.) *Sphincter paralysis, limited anæsthesia.*—Female, aged thirty-six years; had suffered occasionally for five years from endometritis and pains in back and legs, and was suddenly seized at Christmas, 1887, with severe pain in the back and fell to the ground. For several weeks after this she was in bed, and on getting up limped in walking. In April, 1888, she had another attack of pain in the sacrum, and then developed paralysis of the bladder, with retention of urine and loss of sensation below the waist. Three months later the rectum became paralyzed, being emptied with enema with difficulty, though occasionally an involuntary movement occurred. She was first examined by Eulenberg in February, 1890. She then had pain in the back and in the bladder, with tenderness over the sacro-lumbar articulation. There was anæsthesia in the genitals, perineum, anus, and over the region shown in Fig. 12, the dark shading indicating a total anæsthesia. The gait was slow and uncertain, stepping up being difficult, as were also flexion of

the knees and plantar flexion of the feet, the left calf and thigh being weaker than the right and slightly atrophied. Knee-jerks were normal. Achilles reflex lost, and plantar reflex imperfect. No gluteal reflex. All muscles acted to faradism, but it required a stronger current to contract the peronei and ante-tibials than the post-tibials. The bladder was usually emptied by catheter, but spontaneous evacuation occurred frequently. The rectum was beyond control and the sphincter ani was weak. Menses were regular.

Under treatment by strychnine and static electricity there was some improvement, and at the end of four and a half months the anæsthesia was diminished to the limits shown in Fig. 13, the genitals being still affected, this being the region originally of total anæsthesia; there was still imperfect control of bladder and rectum, but the power of the limbs seemed to have returned.—*Zeitschr. f. klin. Med.*, xviii. 547.

These cases seem sufficient to demonstrate that small lesions in the sacral region of the spinal cord may produce limited zones of anæsthesia on the back, thighs, and outer side of the legs, and that the extent and shape of the anæsthesia vary with the extent or situation of the spinal lesion.

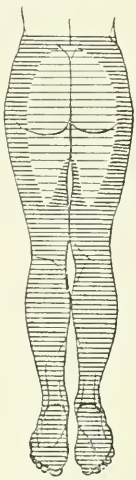
In contrast to these cases the following is of special interest, as it shows that in limited myelitis of the lumbar region the sensory functions of the sacral segments may be preserved and impulses may pass the diseased area of the cord and thus reach the brain.

Case IX. (Starr.) *Central myelitis of the lumbar region, limited anæsthesia; paraplegia.*—The patient, a young married lady, after suffering for some months from backache, was suddenly seized, in May, 1891, with severe pain in the lower dorsal and upper lumbar region, which was much increased by motion and by lying down, and which was soon followed by pain down the left leg in the sciatic distribution. In August, 1891, a swelling appeared at the third lumbar vertebra which gradually disappeared in a month. Its nature is undetermined. On the 8th of August she suddenly lost sensation to heat and to pain in the left leg. On the 16th of September she lost power of motion in the right leg except in the foot. In October the left leg became paralyzed and sensations of touch were also lost. Finally, in November, the right leg became anæsthetic. Early in the disease retention of urine and obstinate constipation appeared and have continued, so that catheterization is necessary. During November the line of anæsthesia advanced slowly upward from the groins to a point half-way to the umbilicus, where it remains.

When she was seen in December, 1891, in consultation with Dr. J. G. F. Holston, there was total paralysis of motion below the waist, including back and pelvis, together with atrophy more marked above than below the knees. All reflex action was abolished. The muscles all reacted to a very strong

faradic current, the reaction below the knees being more prompt than above, and there being normal galvanic response below the knees, and equal response to cathode and anode above the knees. The limbs were flaccid—cool, without rigidity—and the occurrence of bedsores, to which there is a tendency in the back, was prevented by frequent change of position. The loss of sensation to touch, temperature, pain, and muscular sense was absolute below the middle of the lower abdomen and first lumbar spine, but on the back, in a saddle-shaped area of the surface shown in the diagram, Fig. 14, these sen-

Fig. 14.



Starr.

Fig. 15.

Starr.

sations were not lost but only slightly diminished. This area was determined independently by Dr. Holston and myself at different times. This area of sensibility included the anus, perineum, and vagina. The bladder was under no voluntary control, urine being retained till drawn or passed in a stream when the bladder became full, and slight cystitis being present unless the bladder was constantly washed out with borax solution. The sphincter ani offered resistance to the finger. The evacuation of the rectum was difficult with enema, and always painful.

Here there was evidence of a total loss of all the functions of the lumbar segments of the cord, including the first, and of the *integrity of the sacral segments*. Sensory impulses were received in the latter, and made their way upward through the affected lumbar region—a fact which aids the diagnosis, inasmuch as it demonstrates that the myelitis in this region does not affect the posterior columns of the

cord at that part, but must be confined to its gray matter and lateral portions.

The case is stationary at present (April, 1892). In regard to its diagnosis, it is quite possible to exclude a tumor compressing the cauda equina because of the order of appearance of the symptoms: 1, anæsthesia in left leg; 2, paralysis in right leg; 3, anæsthesia in right leg; 4, paralysis of left leg, an order implying the invasion of the spinal cord from its right half over toward its left half, producing at one stage a true picture of a Brown-Séquard paralysis. The possibility of an intra-spinal tumor or gliomatosis cannot be excluded, and it is very likely the cause of the destructive myelitis present. An operation has, however, been advised against, as it seems improbable that an intra-spinal tumor could be removed with any prospect of recovery, the necessary destruction of the cord during the operation being liable to leave as serious results as the tumor is now producing. And the fact that sensory impressions pass up the cord at the seat of lesion indicates that the tumor does not lie on the posterior surface where it might be most easily reached in an operation.

Case X. (Starr.) *Syphilis of the spinal cord; sphincteric paralysis, limited anæsthesia and hyperæsthesia.*—Male, aged twenty-two years (Vanderbilt Clinic, No. 4711), had syphilis in January, 1891, with well-marked secondary symptoms from which he recovered. In November, 1891, he felt some weakness and numbness of the legs. In December, 1891, after dancing all night, found that he could not pass his water and had to have it drawn. At the same time noticed an increased numbness of his legs and felt weak in walking. Felt as if he were walking on a carpet. These symptoms increased gradually and have continued till the time he was first seen (February 11, 1892). Examination showed inability to control his urine, which at times flowed away when the bladder was full, and at all times was retained; constipation, a slight weakness of the legs, exaggerated reflexes and tendency to spastic gait, and a condition of hyperæsthesia to touch, temperature, and pain in area dotted in the figure (Fig. 15), over buttocks and on the outer calf of each leg and an area of anæsthesia of slight degree over the back of each thigh between the hyperæsthetic areas. Under anti-syphilitic treatment and rest he recovered entirely in the course of a month.

The presence of a zone of hyperæsthesia around the body in transverse dorsal myelitis is often recognized. It is interesting to find areas of hyperæsthesia in this case, one corresponding to the area of anæsthesia from lower sacral lesions, one corresponding to the area

of anæsthesia in lower lumbar regions, with a zone of anæsthesia between them.

The diagnosis of syphilis of the cord may be thought indefinite, and it is not impossible that at the time of sudden increase of his symptoms he may have had a slight hemorrhage into the spinal membranes over the sacral cord. But Erb has recently called attention to a peculiar association of symptoms which he considers characteristic of syphilis of the cord, and the patient's symptoms correspond closely to that condition. These symptoms are slight spastic gait and weakness, with increased reflexes but with very little muscular rigidity, interference with the bladder functions, and slight disturbances of sensation, chiefly of the nature of paræsthesia in the legs. There are no symptoms above the waist. The onset is at first gradual, but the symptoms may increase suddenly, and under treatment may pass away. It will be seen that this case corresponds quite closely to this description.

Case XI. (Starr and Lloyd.) *Injury; compression of cauda equina; localized paralysis; sphincteric paralysis; limited anæsthesia; operation; recovery.*—Male; was struck, in April, 1889, on the back while in a kneeling posture, and sustained a fracture of the lumbar vertebræ. He was immediately paralyzed in his right leg; had loss of bladder and rectal control, and a considerable degree of anæsthesia whose area is uncertain. A year later he was seen by me with Dr. Samuel Lloyd.[1] There remained a deformity of the lumbar region most marked at the third lumbar vertebra. There was total paralysis with atrophy and reaction of degeneration of the peronei, anterior and posterior tibial and glutei muscles of the right leg, and some weakness in the muscles of back of the thigh. There was diminished knee-jerk and no ankle-clonus. There was loss of control of the bladder and rectum. There was anæsthesia in the area shown in the diagram (Fig. 16) to touch, temperature, and pain.

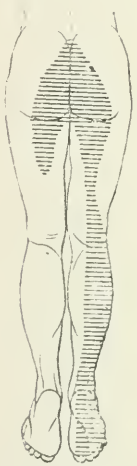
The diagnosis of compression of the cauda equina at the third lumbar level being made, Dr. Lloyd operated and removed the second and third lumbar spines and laminæ. The patient subsequently recovered very slowly but entirely from all his symptoms.

Case XII. (Starr and McBurney.) *Injury; paraplegia, limited anæsthesia; operation; improvement.*—Male; suffered a fracture of the lumbar vertebræ in June, 1891, and was immediately paralyzed in both legs; lost control of his

[1] Dr Lloyd has reported the case in full in The American Journal of the Medical Sciences, July, 1891.

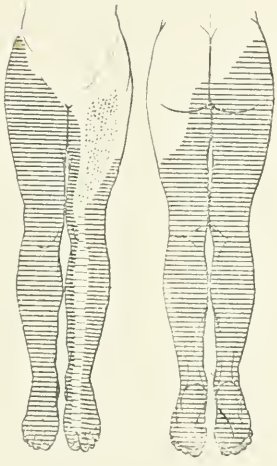
sphincters and had a loss of sensation in the legs. This anæsthesia, he said, was at first as high as the umbilicus and extended about the body, but within a month of the injury decreased slightly and had become permanently limited to the regions shown in Fig. 17. Bedsores developed soon. His condition had been stationary from August to October, when he was seen by me in Roosevelt Hospital at Dr. McBurney's request. I found a total paralysis with reaction of degeneration of all the muscles of the lower extremities, with atrophy, loss of reflexes and of mechanical excitability, the abdominal

Fig. 16.



Starr and Lloyd.

Fig 17.



Starr and McBurney.

muscles, however, being under control and abdominal reflex preserved; complete loss of sensation in the area shown in the figure, to touch, thermic and painful and electric irritation, and an area of marked hyperæsthesia on the left thigh in front over the region dotted. He had no idea of the position of his feet and legs in bed or when moved. He had no control over his bladder, and his rectum was evacuated with difficulty by enemata. He had a deep bedsore over the sacrum, and bedsores on the ankles were prevented with difficulty. The deformity at the first, second, and third lumbar vertebræ was well marked, the second lumbar spine being deflected an inch to the right.

On October 31st Dr. McBurney removed the spines and laminæ of these vertebræ, revealing a fracture of the body of the second lumbar vertebra. The cauda equina was compressed between the body of the vertebra, which had been split off and projected backward, and the laminæ chiefly on the right side. When the cauda was entirely freed, pulsation returned in its

vessels and in the dura. The dura was opened necessarily, and it was evident, from the appearance of the nerve-trunks, that they were degenerated. The wound healed promptly. The bedsores healed within three weeks of the operation. The control of his bladder and rectum had partially returned three months later, but no change in motion or sensation had been produced at the end of six months. He has suffered very greatly from pain in his legs ever since the operation.

The areas of anæsthesia and hyperæsthesia are interesting, and must have been due to compression of the entire cauda equina at the second lumbar nerve, being greater on the right side than on the left. It is evident that the bundles of the cauda lying on the surface on the left side were the only ones to escape.

Conclusions.—There are a number of interesting facts to be drawn from the study of the cases here collected.

First, *as to the location in the spinal cord of the centres of control of the bladder and rectum.* These centres appear to be uniformly affected together, and, therefore, must be adjacent to one another. The control of the sphincters is lost when the lesion involves the lower three sacral segments, and the centres probably lie in the lower two segments of the cord. This is proven by the autopsies in the cases of Kirchkoff, Westphal, Oppenheim, and Herter, and by the distribution of sensory symptoms in two of my cases, and in those of Rosenthal, Bernhardt, Eulenberg, Mills, and Huber. In these cases without autopsy the situation of the anæsthesia was such as to show that the lesion was limited to the two or three lower sacral segments, and in all the control of the sphincters was lost. When these segments are destroyed the sphincter of the rectum is relaxed and there is no opposition to the introduction of the finger into the anus. The entire rectum also loses its power of contraction, so that it is only emptied by pressure from above or by artificial evacuation by means of enemata or excavation.

The sphincter of the bladder does not appear to be permanently relaxed when the cord is destroyed. At any rate a constant dribbling of the urine rarely, if ever, occurs. There is, however, a moderate incontinence, for as soon as a few ounces of urine collects in the bladder the pressure overcomes the slight resistance of the sphincter and the urine flows away. Hence a frequent emptying of the bladder without the knowledge of the patient takes place. There is rarely a sufficient resistance offered by the sphincter to cause a

retention of urine and distention of the bladder when the lesion destroys the bladder centres. This is much more liable to occur when the lesion lies at a somewhat higher level in the upper sacral region and produces an irritation of the mechanism of the bladder. It seems to occur, also, when the lesion involves the cauda equina, producing pressure on the nerve roots. Since pressure upon a nerve elsewhere never produces tonic spasm, this effect must be of a reflex nature from compression of the sensory filaments.

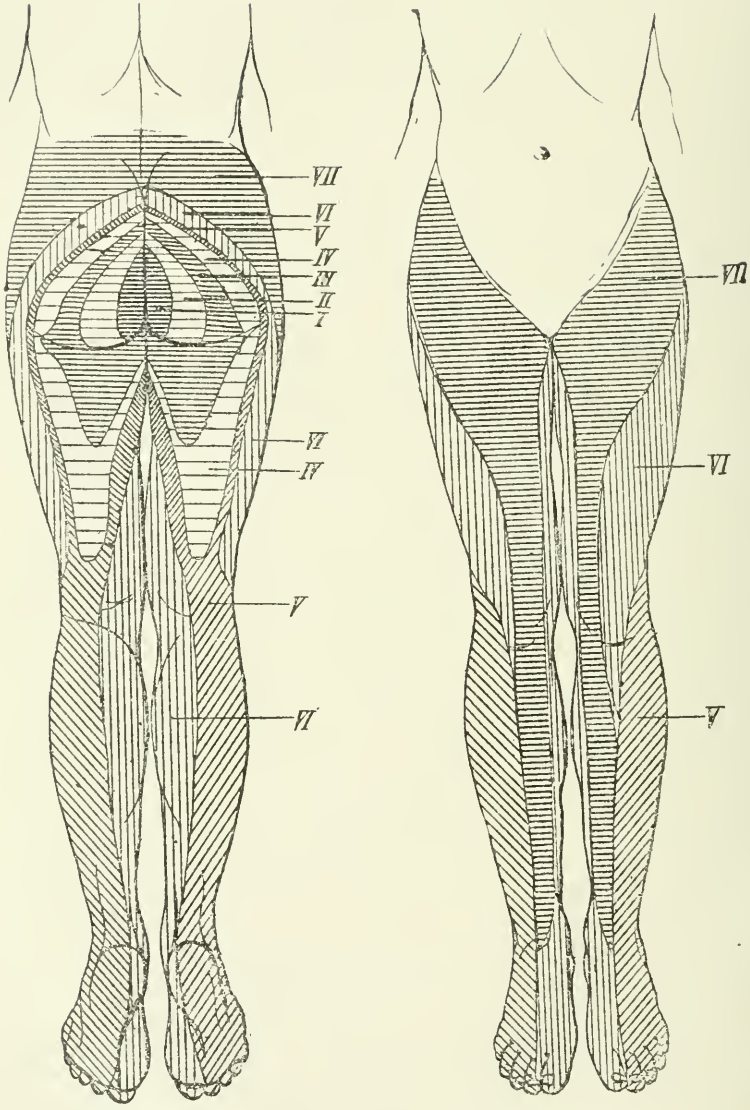
If, in a case of paraplegia, the mechanism of the bladder and rectum is not interfered with—if these organs empty themselves naturally when full—in spite of or without the knowledge or control of the patient, it is a proof that the lesion has not destroyed the lower sacral segments of the spinal cord. In such cases the exact area of anæsthesia should be carefully determined, for the information thus afforded may enable an exact diagnosis of the situation of the lesion and also of the actual extent on the cord to be determined. (See Case IX.)

Secondly, *as to the distribution of anæsthesia in lesions of the lower part of the spinal cord.* This is shown in the diagrams (Fig. 18). These diagrams have been prepared by carefully comparing and superposing the charts of cases cited. In some cases the area of anæsthesia was strictly limited from the outset to a special region. In other cases the area of anæsthesia was large at the outset and gradually diminished in extent. In other cases still the area of anæsthesia was at first small and then increased. The three sets of cases, therefore, must agree in their results, in order to establish any conclusion as to the areas of anæsthesia produced by lesions at various levels. And if the cases here collected be carefully studied it will be seen that they do thus agree. In the diagram of the back it is possible to outline seven concentric zones of anæsthesia, starting from the lowest part of the sulcus between the buttocks as a centre. These are numbered *I.* to *VII.* in the diagram.

I. The *first zone* is oval in shape, small in extent, and includes the perineum, the posterior part of the scrotum in males, the vagina in females; it also includes the mucous membrane of the rectum.

II. The *second zone* is heart-shaped—point up—and includes the entire scrotum and posterior surface of the penis and mucous mem-

Fig. 18.



Areas of anæsthesia in lesions at various levels of the spinal cord from sacral v. to lumbar II.

I. Sacral v.
II. Sacral IV.
III. Sacral III.
IV. Sacral I.
V. Lumbar v.
VI. Lumbar III.
VII. Lumbar II.

brane of the urethra in males—the entire genitals of the female, except the outer surface of the labia majora and the mons veneris.

These two zones can be separated clinically, for in some cases the smaller zone only has been anæsthetic. In the majority of cases the larger zone has been found anæsthetic. No autopsies are at hand to enable a distinction of lesion to be made between these two zones, but from the cases of Kirchkoff, Westphal, and Herter it is possible to affirm that the second zone is produced by a lesion involving the conus medullaris and the fifth and fourth sacral segments of the cord.

III. The *third zone* is considerably larger, involving a greater surface of the buttocks and extending down the back of the thighs over a triangular area, point down. This has been named the "saddle-shaped area," coinciding about with the surface of the seat in contact with the saddle when riding. A zone of anæsthesia of this shape is due, as the autopsy in Oppenheim's case shows, to a lesion involving the fifth, fourth, and third sacral segments.

IV. The *fourth zone* is of a similar shape to the third, but more extensive, a greater surface on the back of the thighs being involved, and the anæsthesia extends in a band almost as low as the popliteal space. This area has been established clinically in several cases: there is as yet no autopsy to determine its lesion; but since the smaller zone is due to lesion at the third sacral segment, and the next larger zone is due to lesion in the fifth lumbar segment, it is allowable to conclude that this region corresponds with the second and first sacral segments.

In thus outlining four zones of the skin and assigning them to various segments of the sacral portion of the spinal cord, it is not my intention to lay down artificial boundaries or to affirm that all cases will exactly coincide. The lesions in the sacral cord are not limited exactly to one or two segments. The sacral cord is small in extent and lesions involve it to a greater or lesser degree, consequently these zones are not always symmetrical on the two sides of the body; the lesion being a little higher on one side of the cord than on the other, the zone of anæsthesia will be greater on one thigh than on the other, as in my first, fifth, and sixth cases, and in those of Herter, Mills, and Osler. I only wish to show that as the cord is invaded by disease from below upward, the area of the skin which becomes anæsthetic increases in extent, and that the shape of

the area is characteristic; so that from the study of the area the extent of the lesion can be determined.

I also desire to call attention to the fact observed in my fourth case, that this area of the skin which corresponds to the sacral cord may remain sensitive in a lesion of the lumbar cord, when that lesion is so limited in extent as not to cut off impressions passing from the sacral cord to the brain. This affords an important evidence of the extent of a lesion in the lumbar cord. For if that lesion is transverse and involves all the columns, all sensation below its level will be lost, while, if the lesion is limited and does not affect the posterior columns of the cord through which impulses are passing up from the sacral region, the total anæsthesia will not include the parts of the skin related to the sacral cord.

Another conclusion of some importance is brought out from a study of these facts, viz., that in locomotor ataxia the lesion probably begins quite uniformly in the lumbar cord, and not in the sacral cord. In a review of about fifty cases of locomotor ataxia, of which I have careful records, I find that the lightning pains of the initial stage and the hyperæsthesia especially to cold, which accompany them, are rarely referred to the buttocks and seat. They are quite uniformly referred to the feet or to the legs below the knees or to the front and outer sides of the thighs. Pain in the rectum, it is true, may be felt. In one of my cases the initial paræsthesia and anæsthesia occurred in the rectum and perineum, the complaint for several months being of a feeling as if a large cannon-ball were lying on the perineum. But such localization of pain and paræsthesia is the exception. If, however, the lesion of locomotor ataxia began in the sacral portion of the cord, it is reasonable to suppose that the sensory symptoms would be referred to the region of the body corresponding to that part of the cord, and that bladder disturbance would be the first symptom. It seems, therefore, quite probable that the lesion in locomotor ataxia begins in the lumbar region—a fact to which the early loss of knee-jerk also points. This may have a bearing on the disputed question as to whether locomotor ataxia is a true "system disease."

The area of anæsthesia produced by lesions in the lumbar cord is also determined by these cases and shown in the diagram.

V. The *fifth zone* of anæsthesia is seen to include the first four

zones and to extend down the back of the thigh through the popliteal space in a band, and then to descend the outer surface of the leg to the foot. In some cases it ends at the ankle, in others it involves the entire side of the foot, dorsum, and sole, and three and a half toes. Eulenberg's case, cases of Kahler[1] and Mills[2] not cited here, and my second and fifth cases demonstrate this distribution When a lesion extends from the sacral into the lumbar cord the anæsthesia extends from the thigh down the outer side of the leg. This area then corresponds to the fifth lumbar segment of the cord.

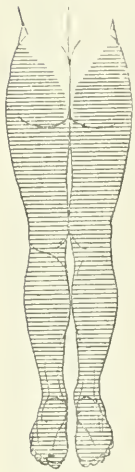
VI. The *sixth zone* of anæsthesia is produced by a lesion of the third lumbar segment. When the third lumbar segment is diseased the entire back of the thighs and legs is anæsthetic and the front of thighs is also anæsthetic, except over a funnel-shaped zone which extends from above downward, the narrow tube of the funnel reaching along the shin even to the foot. This distribution of anæsthesia is well shown in Fig. 17, where the sensitive area in the midst of the anæsthetic zone is well defined. This zone will probably be separated later into two separate parts corresponding to lesions of the fourth and third lumbar segments. There is not as yet a sufficient number of cases to warrant such a distinction. The exact limits of anæsthesia on the feet are still uncertain, and no more exact statement than that given is warranted. It is quite common to find the inner arch of the foot sensitive when the toes and heel and entire dorsum are anæsthetic, and it is probable that the higher the lesion the greater the anæsthesia on the foot.

VII. The last and *largest zone* of anæsthesia shown in the diagram is produced by a lesion of the four lower lumbar segments, that is, by destruction of all but the first lumbar segment of the cord. It will be noticed that the line of anæsthesia is much lower in front than behind, and that it follows the line of Poupart's ligament. It is only when the first lumbar segment of the cord is invaded that the abdominal wall becomes anæsthetic. From this level upward the zone of anæsthesia extends around the body in a girdle, and there is no difficulty in locating the level of the lesion in the dorsal cord.

[1] Kahler: Prager med. Wochenschr., 1882.
[2] Mills: Med. News, March 1, 1890, Case I.

It is to be remembered that in all these lesions and areas of anæsthesia, the *anus, perineum, and the genitals are included in the insensitive region.* This is an important fact in the differentiation of cases of organic from functional paraplegia. It is also to be noticed that the shape of the area of anæsthesia in the back differs in organic and in functional cases.

Fig. 19.



Charcot.

Charcot[1] and his pupil, Souques,[2] have described the area of anæsthesia in hysterical paraplegia, in paraplegia produced by hypnotic suggestion, and in the analogous form of functional paraplegia occurring after railroad and other injuries, and included under the general name of traumatic neurosis or traumatic hysteria. Fig. 19 shows Charcot's diagram. He says:

> "In front the limit of anæsthesia is represented by a line which follows the fold of the groin on each side to the anterior spine of the ilium, *exclusive of the genital organs;* on the back the line follows the insertion of the muscles of the buttocks exclusive of a V-shaped area over the sacrum."

It will be noticed how entirely different this area of anæsthesia is from that due to any of the organic lesions described here. And the escape of the genital organs in the functional cases is also a most important point of diagnosis between hysterical and organic paraplegia.

The study of the area of anæsthesia, therefore, not only enables us to reach a diagnosis of the level of the lesion, but it also enables us to separate organic cases of spinal-cord disease from functional and hysterical cases of a paraplegic kind.

Multiple neuritis is sometimes attended by anæsthesia of the extremities. The anæsthesia is limited, however, to the hands and feet, or if it extends up the limbs it is limited by a line drawn around the legs or forearms below the knees or elbows. It never resembles in its distribution the area of anæsthesia produced by lesions of the spinal cord. Nor can the anæsthesia from injury of special nerve

[1] Charcot: Œuvres complètes, iii. p. 448.

[2] Souques: Iconographie de la Salpêtrière, iv., 1891.

trunks be confounded with that due to spinal disease, as a reference to any diagram of the distribution of the cutaneous nerves will show.

THIRDLY, in cases of transverse dorsal myelitis with a zone of anæsthesia about the body, there is usually present a zone of hyperæsthesia just above the zone of anæsthesia. An analogous condition has been observed in cases of lumbar and sacral myelitis, as shown by three of my own cases (Cases V., X., XII.). But in these cases the region of hyperæsthesia was situated in the area of the surface corresponding to the segments of the cord just above the lesion. In Case V. the area of anæsthesia corresponded to a lesion of sacral V. and IV., the area of pain and hyperæsthesia corresponded to sacral III. As the disease extended the zone formerly hyperæsthetic became anæsthetic. In Case X. the area of anæsthesia corresponded to a lesion of sacral III. and IV.; the hyperæsthesia corresponded to sacral IV. and V. below, and to sacral I. above. In Case XII. the area of anæsthesia corresponded to a lesion of lumbar III. and below it; while the area of hyperæsthesia on the left side corresponded to the funnel-shaped area belonging to lumbar II. Thus the study of the areas of hyperæsthesia confirms the conclusions reached from a study of the areas of anæsthesia.

It may be affirmed that in lesions of the lower cord an area of hyperæsthesia will be usually discovered in the part of the body corresponding to the segment of the cord just above the lesion. And when a lesion is extending the area previously hyperæsthetic will become anæsthetic. If the diagram be consulted, some conclusion regarding the extent of any given case can be drawn from a study of the relative positions of the areas of hyperæsthesia and anæsthesia.

LASTLY, a few words must be added regarding the differentiation of lesions of the spinal cord from those of the cauda equina. The study of the anæsthesia alone does not aid very greatly in the differentiation. A lesion of the sacral nerve roots produces an identical area of anæsthesia as a lesion of the sacral cord. It also produces a paralysis of the bladder and rectum. Thorburn[1] has proved that pressure exerted on the cauda equina affects the nerves in the middle of the cauda to a greater extent than those near the surface.

"Those nerves which pass out lower down are, in the cauda, situated nearer the middle line than those which pass out above them, and hence they

[1] The Surgery of the Spinal Cord, p. 99.

would appear to have more room to escape from pressure, and we might expect them to suffer less rather than more; but that the contrary is the case is an established fact, and we are able definitely to conclude that in a pressure lesion of the entire cauda equina those nerve roots which emerge lower down are more seriously injured than those above them."

This conclusion has been proven by the autopsy in Herter's case, where the middle roots only were degenerated, though the pressure was exerted on all the roots at the level of the last lumbar nerve.

There is no way, therefore, of determining by a study of the anæsthesia alone a pressure lesion on the cauda high up from a destructive lesion in the cord at its lowest extremity. The diagnosis may, however, be made, first, from a study of the surgical indications, chiefly of the nature of deformity, the relation of the vertebræ to the segments of the cord being remembered. The cord ends at the first lumbar vertebra, hence any fracture below that is necessarily compressing the cauda equina. Secondly, the diagnosis may be made from a study of the paralysis which accompanies the anæsthesia. This paralysis is very slight in lower cord lesions, being confined to the peronei muscles when the lesion is at or below the second sacral segment; it involves the anterior tibial and posterior tibial muscles when all the sacral segments are involved, and only invades the movements of the hip-joint when the entire lumbar region of the cord is affected.[1] In cauda lesions, on the other hand, the pressure on the nerve roots is often sufficient to produce widespread paralysis when sensation is but slightly affected.

The cases in which autopsy or operation has revealed the nature of the lesion in diseases of the lower cord demonstrate, however, that a sharp differentiation between cauda equina and cord lesions is not often justifiable. In the four autopsies here cited, both cord and cauda were invaded by the lesion, which was a meningo-myelitis with hemorrhage, the result being a destruction of the lower cord and a matting together of the nerves of the cauda in a mass of inflammatory material. It seems, therefore, questionable whether, except in cases of fracture below the first lumbar vertebra with displacement of the vertebræ, any sharp line of distinction between cord and cauda lesions should be attempted.

[1] For more precise statements see "Syringomyelia," The American Journal of the Medical Sciences, 1888.

It is chiefly in the surgical cases that operative interference has been attempted, and here, as already stated, the surgical rather than the medical facts have been the surest guides to the operation. There is one case on record, however, of successful operation for removal of a tumor compressing the cauda equina (Laquer, *Neurol. Centralbl.*, 1891, x. 193). In this case the extreme pain in the sacral region and the tenderness over the sacral region appear to have been the particular symptoms which guided the operator; the tumor was extra-dural, and the nervous symptoms were by no means such as to suggest a lesion of the spinal cord. In two other cases of tumor of the cauda equina—viz., those of Simon (*Arch. f. Psych.*, 1875) and Lachmann (*Ibid.*, 1882), the characteristic nervous symptoms of compression of the cauda were wholly wanting, and the cases were not diagnosticated during life.

Some writers upon the differential diagnosis between cord and cauda equina lesions have laid stress upon the fact that sensations of touch, temperature, and pain are not always equally destroyed, and have sought to conclude that this inequality of sensory disturbance was evidence of cord lesion as distinguished from cauda equina lesion. The cases here cited of Herter and Oppenheim, with autopsies, and two of my cases, in which the operation showed the lesion to be a compression of the cauda without lesion of the cord, prove that this point of differential diagnosis is not well taken. In both cord and cauda lesions the disturbance of tactile sense may be more or less extensive than that of the sense of pain and temperature.

It is evident from the facts here presented that a careful study of disturbances of sensation is a valuable aid in the diagnosis of the situation of lesions in the spinal cord and cauda equina. It is, however, to be remembered that anæsthesia is but one of a series of symptoms entering into that diagnosis, and the condition of reflexes, and the power, tone, and electric reactions of the muscles are not to be neglected in the examination of any case. It is only when *all* the signs of a local lesion coincide that the diagnosis is an absolute one.

DISCUSSION.

Dr. Weir Mitchell: I have been much interested in Dr. Starr's paper and think the precision of his observations of value. I have only one critical remark to make, and that is regarding the distribution of anæsthesia in hysterical paraplegia. I doubt the accuracy of Charcot's statement and am quite sure that I have seen more than one—perhaps two or three—cases in which there was anæsthesia of the genital organs and perineum, and in which the limitation of the anæsthesia on the back was not such as is shown in Charcot's diagram. I think the statement made that in hysterical paraplegia the genitals are not anæsthetic is not to be taken as an absolute one.

Dr. Miles: In the case that I recorded some years ago of injury to the cauda equina there was a distinguishing mark, from the fact that the wasted muscles of the extremities showed loss of Faradic contractility and degenerative reaction.

Dr. Starr: I am very grateful for the information given to me by Dr. Mitchell. My observation of cases of hysterical paraplegia has been very limited, and this statement which comes from Dr. Mitchell is a very valuable one, and would modify decidedly the conclusions that I had drawn, based upon Charcot's statement.

I regret to say that I cannot see the reason for differentiating in Dr. Miles's case the cauda equina from the cord lesion by the presence of the reaction of degeneration. In cauda equina lesions, of course, we get the reaction of degeneration; in lower-cord lesions we also get the reaction of degeneration. I cannot regard that as a point of differential diagnosis between cord and cauda equina lesions.

Dr. Miles: The patient got well, which proved that it was a lesion of the nerves.

A STUDY OF THE SEASONAL RELATIONS OF CHOREA AND RHEUMATISM FOR A PERIOD OF FIFTEEN YEARS—1876 TO 1890 INCLUSIVE.

By MORRIS J. LEWIS, M.D.,

ATTENDING PHYSICIAN TO THE ORTHOPÆDIC HOSPITAL AND INFIRMARY FOR NERVOUS DISEASES, THE PENNSYLVANIA, AND THE CHILDREN'S HOSPITALS, PHILADELPHIA.

THE present study is a continuation of a former paper upon the same subject read before the Philadelphia Neurological Society, October 25, 1886, published in the *Medical News* of November 13, 1886, and includes the *months of onset* of 1383 separate attacks of chorea, and 673 separate attacks of acute inflammatory rheumatism. Of the former, 717 are from the note-books of the *Philadelphia Orthopædic Hospital and Infirmary for Nervous Diseases*, and include the 436 attacks reported in the paper alluded to; the 281 new attacks having been carefully extracted from the records for the years 1886–90 by my friend Dr. Charles W. Burr, to whom I am indebted for much assistance in the preparation of this paper. The remaining 666 cases occurred in Boston, Mass., and have been collected for me through the kindness of Dr. James J. Putnam and Dr. Philip Coombs Knapp, of that city, from the records of the City Hospital, and the Massachusetts General Hospital, respectively. The 673 separate attacks of acute inflammatory rheumatism have been collected from the records of the Pennsylvania Hospital, for the years 1876–90.

My intention was to collect statistics of these two diseases from several cities widely separated geographically, but I found that these records could not be obtained.

The weather records were extracted from the monthly reports of

the Signal Service Bureau, and furnished through the kindness of the Washington and Philadelphia offices.

Sufficient of interest has been found to warrant this extended study, which was not undertaken to substantiate any particular theory, but to prove or disprove the results obtained in my former paper, where it was considered that a close relationship existed between the number of attacks of these two diseases and the number of storm centres per month passing within 400 miles of Philadelphia.

In the present study, as in the former, the "storm tracings" were obtained by taking the number of tracks of centres of low barometer passing within 400 miles of the localities studied, the 400-mile radius having been previously found to furnish the tracing most closely resembling that of chorea. The tables are so arranged that by the repetition of the first half of the year any portion of any one tracing may be studied in unbroken sequence.

Certain sources of error must be alluded to, and, although at present it is impossible to entirely eliminate them, it is not considered that the final result is thereby vitiated.

1st. The attacks recorded are but a portion of those occurring in the localities studied, while the meteorological data are complete as far as they go.

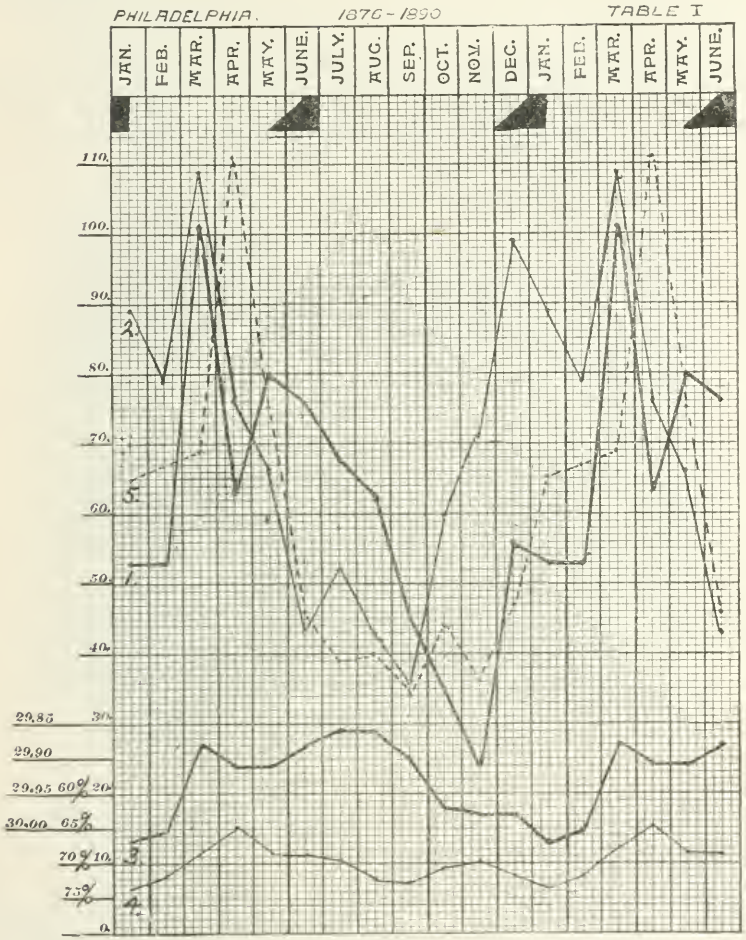
2d. The division of the year into months of unequal length is unfortunate but unavoidable, and all the numerical tracings, therefore, show a tendency to conform to this monthly irregularity; but even this does not vitiate their accuracy, as a reduction of the figures to a supposititious monthly length of thirty days does not materially alter their peculiarities.

3d. Monthly *averages* tend to obliterate daily peculiarities and variations, for by taking the monthly mean of any element the very effect we wish to study may be smoothed out. This is further accentuated when monthly means for many years are taken.

4th. The methods of recording the tracks of centres of low barometer (storm centres) are, in the language of the weather reports, "approximately correct" only.

5th. Much difficulty has been encountered in obtaining definite answers as to the exact time of onset of the attacks. A large number of cases have, therefore, been discarded on this account, and only those retained for study that were apparently beyond doubt. This

objection probably pertains less to the records of the Orthopædic Hospital and Infirmary for Nervous Diseases than to hospitals in

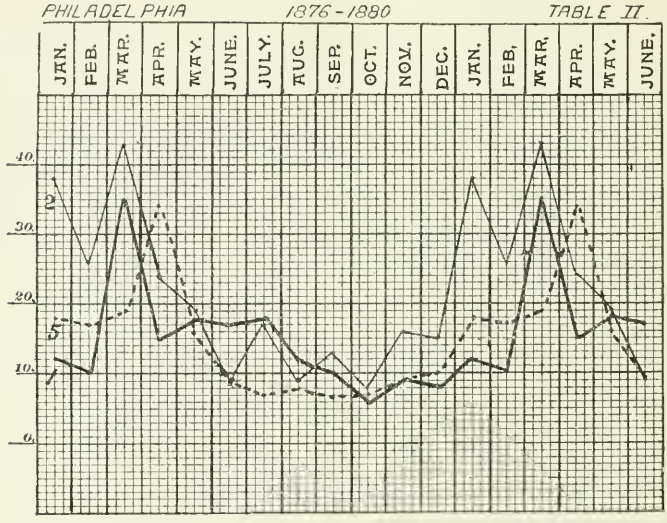

PHILADELPHIA. 1876-1890 TABLE I
JAN. FEB. MAR. APR. MAY. JUNE. JULY. AUG. SEP. OCT. NOV. DEC. JAN. FEB. MAR. APR. MAY. JUNE.
110. 100. 90. 80. 70. 60. 50. 40. 30. 20. 10. 0.
29.85 29.90 29.95 30.00
60% 65% 70% 75%
1. 2. 3. 4. 5.

1. 717 separate attacks of chorea.
2. Storm centres passing within 400 miles of Philadelphia.
3. Mean barometer.
4. Mean relative humidity.
5. 674 separate attacks of acute inflammatory rheumatism.

general, owing to the unusually accurate method of taking histories on blanks printed especially to investigate the various nervous diseases, the exact date of onset of chorea, for instance, being one of

the points particularly investigated. A failure to note this point correctly would naturally have a tendency to cause the case to be recorded as originating later on in the year than was actually the case.

6th. "Habit chorea," as far as the Philadelphia statistics are concerned, has been excluded from the list, but the cases due to *fright* have been unfortunately included with those due to other causes.

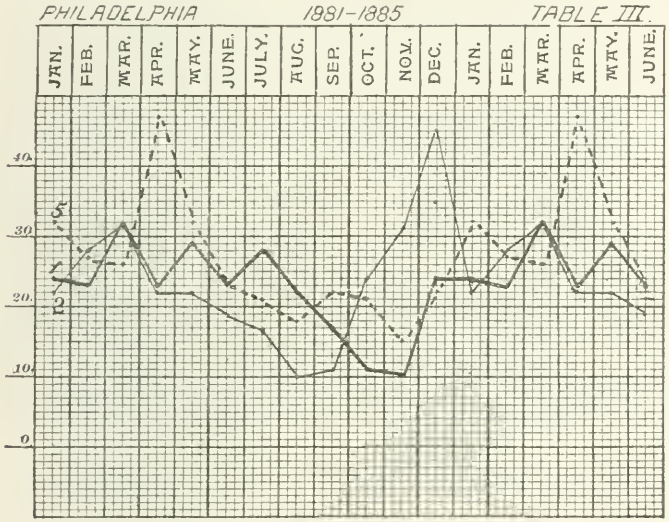


1. 170 separate attacks of chorea.
2. Storm centres.
5. 161 separate attacks of rheumatism.

Table I. represents the data for Philadelphia for the fifteen years investigated, viz., 1876–90 inclusive.

Tracing 1, of this table, represents the months of onset of 717 separate attacks of chorea. It will be seen that November shows the fewest attacks, viz., 24, or 3.3 per cent.; a rapid rise occurs in December to 56, or 7.8 per cent. The tracing remains almost stationary during January and February, and then suddenly reaches its highest point in March, viz., 101, or 14 per cent. A fall occurs in April to 63, or 8.7 per cent.; a rise in May to 80, or 11.1 per cent., and then the tracing falls almost steadily to its lowest point in November.

When this period of fifteen years is divided into three periods of five years and separately studied, the same character of tracing is still observed in each. See Tables II., III., and IV. The latter table is the most irregular, although still possessing many of the same features shown in II. and III. Turning to the records obtained in Boston for the same period of fifteen years (Table V.), it will be found that of the 666 attacks there depicted (Tracing 1), the fewest also occur in November, viz., 30, or 4.5 per cent., although September, with 31 attacks, or 4.7 per cent., is practically the same.

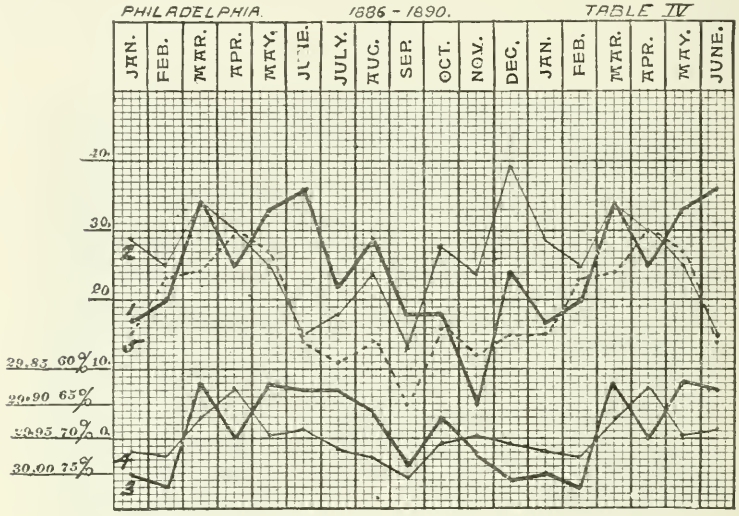


1. 266 separate attacks of chorea.
2 Storm centres.
5. 306 separate attacks of rheumatism.

The line then rises, with a slight break in February, to its highest point in April, viz., 96, or 14.4 per cent., and then falls regularly and steadily to its lowest point in September and November.

The chorea record for Boston for the five years ending 1890 shows a somewhat different character of tracing (Table VI., Tracing 1, representing 357 cases). The months of March, April, May, and June are all practically alike—varying from 43 to 45 cases, 12 per cent. to 12.6 per cent. A fall then occurs, as before, to the lowest point in November, viz, 11 cases, or 3.1 per cent. This table

includes 125 cases from the records of the Massachusetts General Hospital, the remainder being from the City Hospital records. The irregularity of the tracing is due to the cases from the latter hospital, as those from the Massachusetts General, when taken alone, give a record very similar to the general tracing which pertains to Philadelphia, the high period being in March, 20 cases, or 8.8 per cent.



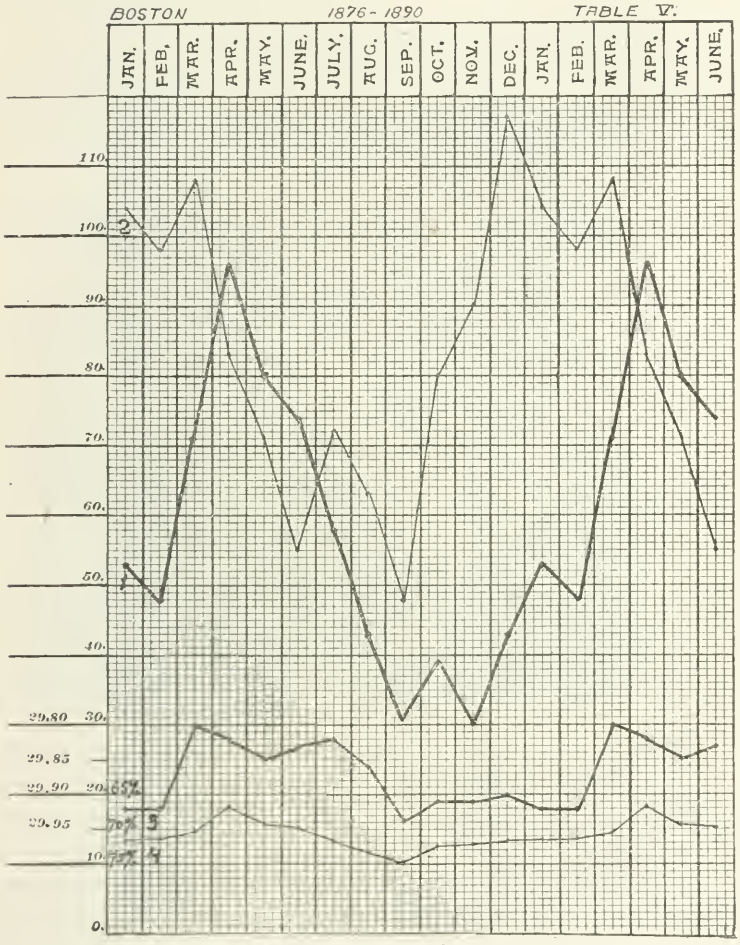
1. 281 separate attacks of chorea.
2. Storm centres.
3. Mean barometer.
4 Mean relative humidity.
5. 206 separate attacks of rheumatism.

The cases from the City Hospital show the greatest number in April. In regard to these cases Dr. Putnam writes me as follows:

"I had not this particular investigation in view when the record of these cases was made, so there may be some errors. The time of onset was sometimes given as 'two months ago,' that is, two months before the time I saw the patient. In all probability the mothers of the children would more likely have understated than overstated the duration of the disease."

An error in this direction, as previously stated, would naturally place the dates of onset of the attacks later on in the year than they should be.

Adding all the cases together, month by month, gives the following result: January, 106; February, 101; March, 172; April, 159;



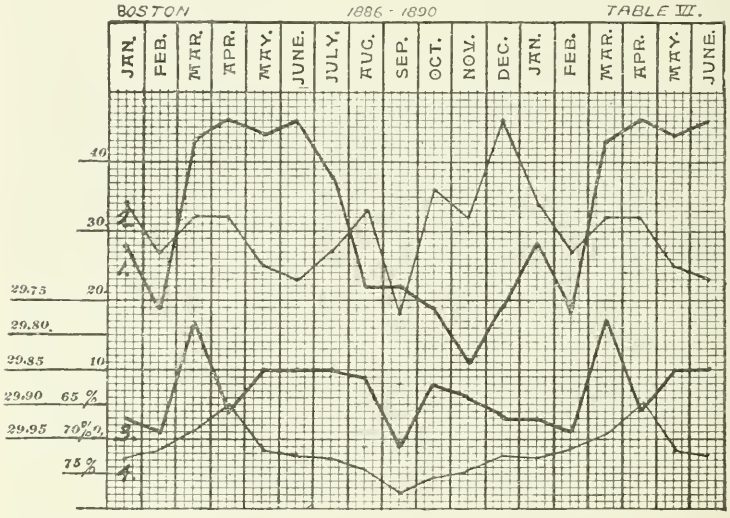
1. 666 separate attacks of chorea.
2. Storm centres.
3. Mean barometer.
4. Mean relative humidity.

May, 160; June, 150; July, 126; August, 106; September, 76; October, 74; November, 54; December, 99. Total, 1383.

This study of the largest number of attacks of chorea that, as far

as I am aware, has been collected together, should prove the fact already noticed, by several observers, notably, Drs. Mitchell, Gerhard, Knapp, and Putnam, that chorea in the United States is essentially a disease of the spring, and that the fewest attacks occur in the autumn. So far, the *seasonal* relation is proven.

In order to see whether this spring augmentation was noticeable in the prevalence of disease in general, I have investigated the time of year when the greatest amount of sickness occurs in Philadelphia.



1. 357 separate attacks of chorea.
2. Storm centres.
3. Mean barometer.
4. Mean relative humidity.

In my own practice, which is a general one, I find that the most visits are paid in March, viz., 15.3 per cent., and that from that point the percentage of visits falls to midsummer (absence of patients from city largely influences this fall); then gradually rises to January to 13.3 per cent.; falls in February to 10.5 per cent., and rises to its highest point in March. This varying percentage I find is about the same as regards the practice of other physicians whom I have interrogated concerning this point, and might be considered by some as a sufficient cause to explain the March rise in the Philadelphia

chorea tracing, upon the theory that March is the month when most disease occurs; but might I not pertinently ask the question, What causes this March rise in the amount of disease?

Over-study has been considered by many to be one of the most potent causes of chorea. Sachs states (Keating's *Encyclopædia of Diseases of Children*, vol. iv.) that "many of the attacks occurring in early autumn follow upon the opening of school, and that in March the strain of winter duties is greatest;" and Sinkler (Pepper's *System of Medicine*, vol. v.) states that "the annual examinations in our schools give a number of cases of chorea." Upon inquiry I find that examinations in the Philadelphia public schools take place in the early part of January and in the latter half of June, and that preparatory reviews begin six weeks previously; that in February and March, the earlier months of the term, the pressure of study is very light; May being the hard month on account of the preparations for the final examinations in June. In the normal schools, where the average age of the children is over fourteen years, the pressure of study in April and May is said to be severe, but it is not probable that any considerable number of these children are included in this study, as the public schools certainly furnish the vast majority. I have endeavored to express graphically, by the wedge-shaped figures on the top of Table I., the time of the semi-annual examinations—the increasing width of the figure representing the increasing pressure of study during the reviews until the examination period is reached.

If over-study is the main exciting cause of chorea, why does the tracing reach its highest point in March, midway between the examinations, when no reviews are taking place and the study is light? Or, if this March rise is the after-effect of the hard work during the midwinter examinations, why does the tracing fall from its moderately high point in May as the final, and hardest, examinations of the year are approached? It is true that as the December reviews and the January examinations draw near there is a rapid rise in the number of attacks; but here again a slight fall in the tracing is seen *during the examination period*, when the worry might be supposed to be at its height.

The children with chorea applying at the Infirmary belong to an unusually intelligent class of society, and are themselves intelligent;

as a rule, they are quite anæmic, and it is undoubtedly difficult to determine how much over-study has contributed to bring about this result and the exaggerated nervous susceptibility accompanying it.

The next etiological factor to be studied is the weather.

The "weather," using the word in its broadest sense to express the varying atmospheric and electrical phenomena which we call weather, is a strangely complex whole, which is exceedingly difficult to reduce to lines and figures.

It was thought that the record of "centres of low barometer," or "storms," as they occurred month by month, would, on account of the fact that a "storm" of necessity includes many meteorological factors, more fitly than any other series of figures represent the deleterious elements of "weather," but the present study does not entirely uphold the conclusions previously drawn in regard to this point. In Table I. the storm line (Tracing No. 2) is singularly like that of chorea (Tracing No. 1) for the same period, in its general configuration, but there is a considerable lack of correspondence between them in summer and autumn; in the former the chorea line rises much higher, and in the latter falls much lower, than would be expected did the storm tracing express the true etiological factors of this affection. Were the thunder-storms, which nearly all occur in summer, included in the storm tracing, the latter would be considerably augmented at the point where, upon this theory, there is the unexplained rise in the chorea tracing. The Tables II., III., and IV., all show this same overlapping of these tracings in summer and winter.

In my former paper I made use of the following expression:

"Anyone looking at these two tracings, as shown in the chart, will have to acknowledge that the marked resemblance which exists is more than accidental, but to decide which factor in this complex disturbance, which we call a storm, is the baneful one, or in what manner it acts, is difficult."

This conclusion was reached after studying the tracings for the years 1876–85 inclusive (which may be reproduced by adding together Tables II. and III.). In the present study the addition of 281 more cases for the five years 1886–90 inclusive, does not, as we have seen, materially alter the general configuration of the tracings; but upon dividing the whole number of attacks into periods of five years each, and studying them separately, it will be found that the

last series (Table IV.) shows but a partial resemblance between the chorea and storm tracings. For instance, June shows the highest point reached by the chorea line, viz., 36 attacks, or 12.6 per cent., while the storm curve is almost at its lowest point, so that an element of doubt necessarily arises as to whether the principal exciting cause has been determined.

At this point of the study the thought arose that if the chorea and weather statistics for the same period of time, of several localities far apart, could be studied and compared, something of interest might be forthcoming, and the proper etiological value of weather influence determined. The only statistics that could be obtained, after considerable effort, were those of Boston, kindly furnished me by Drs. Knapp and Putnam.

Table V., Tracing No. 1, shows the tracing obtained from the study of these 666 cases of chorea occurring in Boston during the fifteen years 1876–90 inclusive; this tracing has been previously described. The storm tracing of this table (No. 2) resembles in its general aspect the corresponding tracing for Philadelphia (Table I., No. 2), the two maxima and minima coinciding exactly, as would be expected; but on comparing it with its accompanying chorea tracing, the resemblance between them is not as pronounced as is seen in Table I., and there is a greater exaggeration of the winter dissimilarity previously alluded to. When the storm tracing for Boston for the years 1886–90 inclusive (Table VI., No. 2) is compared with its accompanying chorea tracing (No. 1), previously described, for the first time but little resemblance is seen between them.

Unable to find a satisfactory explanation that will cover all cases, in the storm tracings, I again turned to the records of the mean actual barometer and mean relative humidity. On this point I previously remarked "that there appears to be an increase in the number of attacks of chorea with a fall of the mean relative humidity and barometer tracings." To make these tracings more intelligible they have been reversed in the tables, so that any relationship between them and the other tracings may be more readily detected.

Naturally some resemblance might be expected to exist between these tracings and that of the storm centres, as they are component parts of the storm disturbance. The rise and fall of the barometer tracing (No. 3) in the various tables bears a considerable resemblance

to that of chorea, and this is particularly noticeable in Tables IV. and VI., where the resemblance of the storm to the chorea tracing is least marked. It must be borne in mind that Tracings 3 and 4 are reversed, a rise in the tracings really expressing a fall, and *vice versa*. The tracing obtained by recording the number of cloudy or rainy days, and also that by measuring the precipitation in inches of rain and snow, being also component parts of a storm, bear some resemblance to the latter tracing; they are not represented in the tables, as a large number of lines is confusing.

The average monthly temperature steadily rises to its highest point in July from its lowest point in January, and as steadily falls again. The high spring point of the chorea tracing corresponds with cool weather and a *low* barometer and mean relative humidity tracing, but the rise in the autumn corresponds with cool weather and a comparatively *high* barometer and mean relative humidity, the temperature record, therefore, giving us but little information.

Table I. shows the months of onset of 673 separate attacks of acute inflammatory rheumatism occurring in Philadelphia for the years 1879–90. (Tracing No 5.) April has 111 attacks, or 16.5 per cent. A rapid fall occurs until the lowest point in September is reached—34 attacks, or 5.1 per cent.—and from this point the line somewhat irregularly rises until the high point in April is reached. Each of the Tables II., III., and IV. show this same character of the rheumatism tracings and the marked resemblance which they bear to the fluctuation of the storm record, the high point in the latter antedating the month of greatest number of attacks of rheumatism, as if its influence was preparatory, as remarked in my former paper. Unfortunately, no trustworthy records of this disease could be obtained from other cities to compare with those of Philadelphia.

If it is conceded that the relation is positive, as far as cause and effect are concerned, between storm and neuralgia, why may not the same relationship, although possibly to a different degree, be conceded to exist between the varying meteorological conditions and other nervous diseases, notably chorea, which occur in children who are in an unstable nervous condition, depressed in vitality, and possibly over-worked and over-taught?

The conclusions drawn from this paper are as follows:

1st. The seasonal relationship of chorea and rheumatism is proven.

2d. There is a marked resemblance in form between the chorea and rheumatism tracings and the tracing representing the total amount of sickness present in the community per month.

3d. This monthly variation in amount of sickness is not a cause of the fluctuation in the chorea and rheumatism tracings, but is itself probably due to the same influence.

4th. While over-study assuredly plays a most important rôle in predisposing children to chorea, the months of greatest study, and, therefore, presumably of the greatest depression of bodily vigor, do not coincide with, or even precede with any regularity, the months of greatest frequency of this disease.

5th. It is more than probable that "weather" is one of the most important predisposing causes of both of the diseases studied in this paper, although precisely which meteorological factor is the baneful one does not clearly appear. No one element of "weather" explains fully the fluctuations of these tracings for chorea, although in the barometer and storm statistics the relationship appears to be closer than to any other etiological factor or factors that have, as yet, been advanced. It is as if a conclusion was attempted to be drawn from premises, some of which are imperfectly stated or not clearly understood, or possibly even overlooked.

6th. Either this apparently close relationship must be acknowledged to have an important place in the etiology of these diseases, or else the resemblance must be considered to be purely accidental, which seems most unlikely from a study of the tables shown.

More accurate deductions do not appear possible from the data at present at our command.

Explanation of Tables.

In all the tables, Tracing No. 1 represents chorea; No. 2, storm centres passing within 400 miles of the locality studied; No. 3, mean actual barometer; No. 4, mean relative humidity; No. 5, acute inflammatory rheumatism.

Tracings Nos. 1, 2, and 5 are interpreted by using the columns of figures commencing at 0 and ascending regularly by increments of 10; Tracing No. 3, by the figures representing barometer readings; and No. 4, by the figures representing percentages. Tracings Nos. 3 and 4 are reversed.

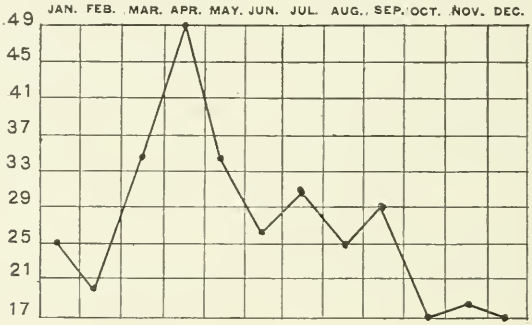
In Table I., Tracing No. 1, represents 717 separate attacks of chorea; in

Table II. it represents 170; in Table III., 266; in Table IV., 281; in Table V., 666; and in Table VI., 357.

Tracing 5 represents, in Table I., 673 separate attacks of acute inflammatory rheumatism; in Table II., 161; in Table III., 306; and in Table IV., 206.

DISCUSSION.

Dr. M. A. Starr: Knowing that a paper was to be read upon this subject, I went over my records of chorea for the past four years at the Vanderbilt Clinic. The points that have been brought up by Dr. Lewis are covered pretty fully by my statistics. I have very accurate and full statistics of 356 cases of



chorea since February, 1888. The tables that the Doctor has presented here coincide quite closely with the chart that I have prepared from these cases of my own. I knew that his statements were to be based upon cases in Philadelphia and Boston, and I thought it would be valuable to have statistics from another source. The number of cases in which I am perfectly certain of the month and day of onset is 325, and of these the largest number, 49, occurred in the month of April. That is just a little later than the Doctor's highest month, the month of March, but it is certainly very close to it. The number in March was 34, the number in May, 34, and the number in April, 49. The curve descends from May down to December, which is my lowest month. My lowest numbers are: October, 17; November, 18; December, 17—making three months virtually the same. In January there were 25; February, 20; March, 34; April, 49; May, 34; June, 26; July, 31; August, 25; September, 29.

A word as regards etiology. It seems to me that over-study is not a very decided cause of chorea. In only 9 of my cases was it the cause. I see a very large number of cases in dispensary practice, and very few among the higher

classes. Certainly study is as hard amongst the higher classes as amongst the lower. I find that 65 cases are decidedly assigned to fright. This would indicate that we must look for a number of etiological factors in this disease; that we cannot trace everything to the weather or to mental work.

As regards the percentage of rheumatism in my cases: I found that 18 per cent. had a distinct history of rheumatism preceding the attack of chorea; 266 cases denied having had rheumatism or growing-pains. The heart was found to be absolutely normal in 199 out of 356 cases. An organic murmur was found in 64; a functional murmur, subsequently disappearing, in 56, and the heart was not examined in 37 cases.

It seems to me that the reason why chorea occurs among the lower classes chiefly, and why it occurs in the spring of the year, is that in the spring those elements which are likely to produce disturbances of nutrition then culminate. During the winter the child has been more or less confined to the house; it has been under more or less physical and mental strain, and has been subjected to all the bad influences which impair nutrition that we find in the tenement houses, and thus we have a sort of culmination in the spring of a number of causes acting together. I think this is to be considered as well as the meteorological cause.

Dr. Weir Mitchell: I want to express my appreciation of this paper, which represents an almost inconceivable amount of labor.

The class of cases we deal with at the clinic of the Infirmary for Nervous Diseases is so much above that of the tenement-house class that the conditions that apply to one would hardly apply to the other. It is the mechanic class, and those a little above them, with which we have to deal, and they live in Philadelphia in an atmosphere of comfort not enjoyed by that class in any other city. I am still in doubt as to the complete etiology of this disease, but think this paper a great advance upon any knowledge we have had hitherto. I hardly believe that mental strain has much to do with the matter.

All the conditions stated by Dr. Starr ought to apply more strongly to the class of blacks than to any others, and yet in Philadelphia, where we have a black population, it is quite well known, and brought out by former researches in my own clinic, that chorea among the blacks is practically unknown. I believe the views of Southerners on this subject agree, on the whole, with our former conclusions. I believe that in England and on the Continent it is the general belief that cases of chorea occur most frequently in the autumn. It would be exceedingly advisable if this paper of Dr. Lewis would arouse them abroad to make some similar inquiry.

Dr. Henry: I wish to call attention to the fact that in studying the relations between chorea and rheumatism it should be borne in mind that there are other manifestations of rheumatism than the articular. For example, there can be no doubt that many cases of tonsillitis are rheumatic, as is evidenced not only by their yielding to the remedies which are so efficacious in

the treatment of rheumatism, but also by their being occasionally followed by endocarditis.

Erythema nodosum is another affection which is believed by many to be a manifestation of a rheumatic diathesis, and chorea has been known to be preceded or followed by this cutaneous disorder.

Dr. Starr remarked that there was a history of rheumatism in but 18 per cent. of his cases, while there were 64 cases of valvular heart disease. This, in my opinion, is proof positive that the percentage of cases of rheumatism is much higher than the figure stated, a figure based upon the presence of articular symptoms alone.

I believe the relation between rheumatism, using the word in its broadest sense, and chorea to be a very intimate one; much more so than appears in Dr. Lewis' tables, although they demonstrate this relationship in a very decided manner.

Dr. Jacobi: I believe that Dr. Starr was correct when he attributed the predisposition to chorea not so much to over study alone as to the combined results of over-study and other causes. As a rule we find that choreic patients are either under-fed, or are hydræmic, or in a condition of ill-nutrition.

We find that chorea is mostly observed at the same time that a number of other diseases are mostly observed—infectious diseases, puerperal diseases, etc. This must be attributed to the fact that at the time the system of every one is run down, not so much by over-work, but because during the winter the windows are not opened; people are less exposed to the influence of fresh air and are more apt to be attacked by whatever disease is epidemic.

As far as the connection between chorea and rheumatism is concerned, to which this accurate and elaborate paper of Dr. Lewis refers, those who remember the older literature on the subject will recollect that it was particularly the French school that attributed chorea minor principally to acute articular rheumatism. From an early time I have been of the same opinion, and I expressed that opinion many years ago in my essay on rheumatism in infancy and childhood, published in 1875 in the Seguin series of *Clinical Lectures*. Since that time the highest percentage of chorea that has been attributed to rheumatism has been 30 to 40 per cent., and that would coincide with the figures of Dr. Starr.

Dr. Henry calls attention to the fact that in Dr. Starr's statistics there were many well-established cases of organic diseases of the heart. That is so. There must have been much rheumatism, for these diseases of the heart in childhood are mostly due to rheumatism, since congenital cases are liable to die in very early infancy. Indeed, there are very few other causes besides rheumatism that give rise to these organic heart troubles in childhood; scarlet fever is only now and then a cause. Why is it that the reports of articular rheumatism differ so much? Simply because a diagnosis is made so seldom. We find a great many cases of rheumatism in children and infants which have not the articular symptoms. I have seen a certain number of cases in which chorea was the first symptom to appear. I have seen three or four cases in

which there was an alternation between choreic and rheumatic symptoms. This would point to the closest relation between chorea and acute articular rheumatism.

The symptoms of rheumatism are sometimes so trifling that nobody thinks that rheumatism is present. The so-called "growing pains" are one of three different things; in very rare cases we have to deal with a neurosis; in a very large number of cases it is an epiphysitis. The pain that we see after typhoid fever or after scarlet fever, the pain followed by a rapid growth of the bone after eruptive fevers, is the result of an epiphysitis. Most cases of "growing pains," however, are those of acute or subacute rheumatism. The so-called "growing pains" that come every few months are often of that nature.

I appreciate very highly the paper of Dr. Lewis for two reasons: first, because there are a number of new facts in it; second, for the egotistic reason that it upholds my own old opinion that rheumatism and chorea belong more to each other than has been appreciated in the past few years.

Dr. Lyman: I wish to express my appreciation of the value and magnitude of the labor that is represented by these plates. I think there is no other paper that has been presented at this meeting that exhibits as much thought and labor.

I wish to add my testimony in the same direction that has already been taken in regard to the connection between chorea and rheumatism. I think we are coming to view in their proper light a large class of cases that are dependent upon what may be called the arthritic diathesis. In my own clinic the experience coincides with that of Dr. Starr, viz., that it is true that the majority of cases are sickly, but are not of a class who are worrying their brains with intellectual research. In almost all cases there is a history of consumption, or rheumatism, or some other cause of debility preceding the outbreak of chorea, not necessarily in the child itself, but a hereditary precession of such causes.

Dr. Jacobi: Chorea is seen so much at that time because then every child, as well as every adult who has no out-door work, is in a condition of ill-nutrition and general constitutional debility, and therefore gives way to every strain upon the nervous system. Therefore, I compare the prevalence of chorea with the prevalence of infectious diseases, which are, also, most common at that time. If that were not so, why should not puerperal diseases be as frequent in other months?

I did not mean to say that chorea and rheumatism belong together in every case. What I do mean is that the two must belong together, because a number of cases of rheumatism that I have seen, and a number of cases of chorea, were simply part of the same affection.

Dr. W. H. Thompson: It is a very easy thing to get a history of fright in these cases, if we suggest to the parents that perhaps their child has been frightened. If fright is an element in the etiology, then the statistics given

us would show that there are more people frightened in April than in any other time of the year.

Dr. Morris J. Lewis: It has just been stated that it is not likely that over-study has much influence in the causation of this disease, as the cases usually come from the least intelligent and intellectual classes of society. I can only repeat that the children coming to the Infirmary with chorea belong to an unusually intelligent class, and are themselves, as a rule, very intelligent.

In my experience with chorea I have seen only four colored children affected with this disease.

The rheumatism records are taken from the Pennsylvania Hospital, and all the cases were adults, while the chorea cases were all children.

Dr. Musser: It has occurred to me that in addition to the explanation presented by Dr. Starr, and with which I am quite in accord, that the difference in the number of cases at different periods of the year might be accounted for in a measure by the diet of these individuals; thus, as we well know, particularly amongst the class of patients subject to chorea and rheumatism, as the winter comes on the class of food changes entirely, and they live largely on starchy foods and meats. As a culmination of continuous starchy diet, the confinement of the winter and bad hygienic conditions, we have the development of the high curve of frequency in these diseases in the early spring. Then as they begin the use of fresh, succulent vegetables, and take more fluids, the curve for these diseases falls. It seems to me that such an explanation is quite as plausible as the one which attributes the greater prevalence of these diseases at certain times to be due to the influence of storms.

THE SIGNIFICANCE OF INTERMISSION IN FUNCTIONAL NERVOUS DISEASES.

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The term functional has been applied in general to those nervous diseases in which no characteristic organic changes have yet been demonstrated. Most writers, however, regard the term as only provisional, on the assumption that some kind of structural change in nervous matter must underlie and be the occasion of every definite nervous disorder; and they, therefore, look to the progress of our knowledge as destined, in proportion to its completeness, to reduce more and more the number of functional nervous disorders, if not finally to enable us to dispense with the term altogether. This view might be allowed to pass unchallenged were it not that in no class of diseases is the subject of treatment so intimately related to etiology as in nervous diseases. If, therefore, there are any reasons to conclude that some disorders of nervous function, very definite in kind and of every degree of intensity, may develop without any departure from the normal in nervous structure, our practical deductions hardly can fail to be influenced materially thereby, for then we may have to look elsewhere than to the nervous system for either cause or remedy. The question, therefore, whether there be any distinctive features which indicate that functional nervous diseases do exist as such, and that these features establish a fundamental difference in them from all affections due to structural changes, is one of more than theoretical interest, and hence I would beg leave briefly to discuss some points which have long seemed to me to show that there are nervous disorders which cannot be explained by any hypothesis of changes in nervous matter, whether molecular or otherwise.

I suspect that the main reason why all specific nervous disorders

are ascribed to some corresponding derangement of nervous texture is because every known organic nervous lesion is always accompanied by corresponding symptoms of functional derangement. It is not only so, but it always must be so. A positive structural change in nervous texture must produce its results in nervous function without fail. But is the converse of this statement equally true, namely, that derangements of nervous function always imply corresponding derangements of nervous structure? I think not, for several reasons, and the first which I would offer for consideration is suggested by the significant difference between two great classes of nervous diseases, namely, those whose symptoms of disordered function are never wholly absent, and those whose symptoms are as constantly intermittent.

Organic nervous lesions, as a rule, easily explain their accompanying nervous symptoms, though sometimes they do not. Frequently they subserve the same purposes as experiments on the lower animals in demonstrating physiological facts or laws. But clinically they are always characterized by one common feature, viz., that their symptoms never disappear except with the disappearance of the lesion. The symptoms accompanying such lesions may vary from time to time, but varying is not disappearing in the sense which belongs to our discussion. What we mean by disappearing is that all signs of nervous disorder, or in fact sometimes of any disorder, are so truly absent in typical cases of certain nervous diseases, that no one would suspect the fact of such disease from any observation of his own made in the interval between attacks. Thus in structural diseases a case of hemiplegia may show a greater degree of weakness one day than another, but he is always hemiplegic nevertheless. A patient with fully developed locomotor ataxia may vary considerably from day to day, but never is he so much better that no one would be able to detect a sign of any disease in him. But in functional diseases the most skilled specialist may be wholly unable to foretell that a man whom he meets in company will terrify a room full of people within an hour by falling in a violent epileptic fit, or that the vivacious lady near him will be prostrated the next day with a severe sick headache.

It is easy to see why this difference between structural and functional nervous diseases should be overlooked, and an anatomical

explanation for the intermittent affections be expected, in view of the great progress during late years in the pathological anatomy of the nervous system. Instead of the macroscopic changes on which our predecessors had to rely for explanation of symptoms, microscopic research, aided by methods of staining and other means of modern technique, repeatedly has substituted scientific certainty for doubtful guessing in nervous pathology. Moreover, our gains have been such in the knowledge of the physiological relations, both peripheric and centric, of the intricate network of nerve fibres by the experimental degenerative methods, and by noting the developmental stages of the nervous tracts in the embryo, that the triumphs of anatomical research in the nervous system must be admitted as both many and great. One by one of the diseases of sensibility or of mobility which our predecessors either could not understand or could not discriminate, are now as clearly demonstrated to depend upon definite organic lesions as a hemiplegia or a compression myelitis. Tabes, lateral sclerosis, anterior poliomyelitis, progressive muscular atrophy, disseminated sclerosis, multiple neuritis, and other degenerative or inflammatory affections are as well defined now pathologically as they are clinically. But, when all this is taken into account, we still ask how much nearer has microscopical research brought us to the solution of our problem? Which of these microscopic lesion diseases intermits any more than a hemiplegia intermits? Even grant that there may be diseases due to molecular, and, therefore, ultra microscopic, changes in nervous matter, how would such changes explain intermission, when molecular changes in every other case are just as abiding as any other changes?

But, without losing further time, we beg to dismiss all reference to molecular hypotheses, on the ground that no definite idea whatever can be connected with this term. It is difficult enough in pure physics to attach a mental conception to this term, as witness the discussions upon what solution is. But when we turn to the living world the difference between two minute specks of protoplasm, one of which is to develop into a great fish and the other into a great quadruped, is doubtless molecular; but how much does our saying so indicate our knowledge about what a thing is when it is molecular? Molecular hypotheses for nervous diseases may be as many as there are imaginations, but our concern is to seek for something which can

come within the range at least of observation if not of demonstration.

On the other hand, the constant postulate that nervous function must always have a textural basis, while partially true, is far from being the whole truth. I suppose that no one will deny that the nervous system constitutes a mechanism in whole and in part. By a mechanism we mean something which is constructed to subserve one or more functions, and by function we mean the specific working of the mechanism. Now structure is not enough for the working of any mechanism, living or non-living. No mechanism is self-working. There is always something plus mechanism needed for working, and that something is a source of energy which will work the mechanism. A lamp, for example, is a mechanism for the function of producing light. Damage its mechanism in any way, as by cutting the wick, or otherwise injuring its structure, and you will correspondingly injure its light-giving function. But you may have the light equally affected while the structure of the lamp is perfectly intact, by not having oil enough, or by mixing with the oil something which will put out the light entirely. The same must be said of any mechanism in the living body, whether muscular, glandular, or nervous. One and all depend for their working, or their functions, upon a constant supply of energy from the circulation. Why, therefore, may we not have functional derangements in the bodily mechanism which are no more due to textural alterations than the disordered light-giving function of a lamp, which, for example, is deranged if water be mixed with the oil, and deranged on that account alone, and not because the lamp's mechanism is even molecularly deranged in any of its parts.

I suppose that no one will dispute this possibility theoretically, but many will dispute its applicability to the explanation of the causation of functional nervous diseases on account of their persistency seeming to imply something more permanent than circulatory disorder to account for them. An epilepsy which lasts for years appears to require a constant fault of condition, which derangements of the blood hardly can be supposed to explain in comparison with the conception of faulty organization. When to this is added the clinical fact that the tendency to most pronounced functional neuroses shows the element of heredity even more distinctly than in the case

of organic neuroses, the presumption of such deep-seated affections being connected essentially with structural causes is rendered very strong.

Our answer to this objection is, that it is based upon as partial a conception as to what the blood is as the other conception alluded to, that nothing is needed for the working, or the function, of a mechanism but the mechanism. This partial conception is, that the blood is a fluid which is nutritive or energizing, and nothing more—that is, a liquid derived wholly from our food supply. A truer conception, it seems to me, is that the blood is a nutritive and energizing fluid, and a great deal more besides, namely, that it is a living tissue as well, owning a living birth and origin as much as the muscular and nervous tissues do. Therefore we may have blood with hereditary faults of development as much as we have nerve-cells or fibres with hereditary faults of development. Family tendencies to blood dyscrasia, whether proceeding from the blood-making or blood-depurating organs, or from faulty development of the blood-cell elements, are as pronounced as any other hereditary tendencies, and, therefore, may be as worth our attention as hereditary structural degenerations. If so, persistency may be as equally predicated in the one case as in the other. The question then becomes, What do the facts of experience indicate? Are the distinctive features of functional neuroses, of which intermittency is one, best explained by the hypothesis of textural changes, which somehow only show their effects now and then, or do they seem best connected with the more easily varied states of the functionating element of the living mechanism?

This question cannot be answered by either humoralist or solidist without discussing first what is meant by the term functional when it is applied to a well-known class of poisons in whose operation we find fully illustrated both the elements of intermittency and of absence of appreciable structural change. Thus the opium eater intermittingly deranges the function of his nervous mechanism for years together; but, however profoundly affected it be with each dose, yet it is afterward as little changed texturally as a steam-engine is by the nightly banking of its fires with ashes. By a proper selection of these functional poisons we can artificially induce some close imitations of functional neuroses, and cause neuralgias, paralyses, delirium,

convulsions, comas, and all intermediate symptoms of the kind, and then note these symptoms disappear in about the time and order that a functional nervous attack develops and declines. The feature of intermittency would then correspond to the intervals of intoxication in this respect, namely, that with analogous periodic doses of opium, for example, we would have recurrent attacks of temporary functional derangements, giving just the same symptoms each time, with no new element developing, the same as functional nervous diseases may recur for years without indicating that ominous feature of progressive extension which goes with most organic neuroses. So close, indeed, may be the resemblance between the occasional action of functional poisons and the intermittent attacks of functional neuroses, that cases of secret indulgence in narcotics may be easily mistaken for cases of functional disease. A little consideration shows that the reason for this close resemblance lies in the element of intermittency, for with the exception of malarial diseases there are no intermittent affections except functional neuroses and cases of functional poisoning, for organic poisons are no more intermittent or temporary in their symptoms than are structural diseases.

The second element of correspondence between functional poisons and functional neuroses is, as already intimated, that in both pathological anatomy affords no assistance in the explanation of the results. By many this deficiency is expected to be made up sooner or later, but in the case of functional poisons there is one important fact which seems to forbid any anticipation of the kind. That fact is this: Functional poisons never affect the whole nervous tissue in the same way, for the simple reason that nervous cells and filaments widely differ in the extreme variety of their functions from muscle or glandular cells which rarely have but one function. Hence, instead of functional nervous poisons affecting all nervous tissue in one way, which may yet be discoverable, they are characterized by a remarkable selective action. Strychnia does not affect the whole spinal cord, and what operation is more limited in the nervous tissue involved than in the case of prussic acid? To experiment, therefore, with cells belonging to the cerebral cortex, or to an abdominal ganglion, would not throw the least light upon the action of either of these distinctive poisons. We should first know the corresponding structural difference between all the different parts of the nervous system which have

different functions before we could tell why this agent so specifically affects the function of one part, and the other agent that of another part. In fact, there is much loose language used in speaking of this or that functional nervous poison as an agent "which acts upon the nervous system." A drug which is a general nervous stimulant or a general nervous sedative is an absurdity, for even the most widely operative of these agents leave a multitude of nerve centres or nerve fibres wholly unaffected by any specific operation of their own. On the other hand, it is on account of their specifically selective operations that each of these agents occasions its special symptoms. Hence, to expect that we may yet be able to tell the difference between opium poisoning and belladonna poisoning, not by signs of changed function but by changes in structure, implies that we will yet know the physical basis of all the different nervous functions. Knowledge of normal function must precede that of disordered function, and not until the anatomical bases of a normal sensation, or of a motor impulse, or of a thought, are demonstrable, can we expect to demonstrate how this functional poison produces delirium and that paralysis.

On the other hand, precisely the same selective action confronts us in the phenomena of those diseases which, though they may be terribly fatal, yet leave nothing for morbid anatomy to explain. Thus I have had two cases of Landry's paralysis to observe, with in each exactly the same selective action illustrated in the parts affected as with strychnia itself.

The third feature of correspondence is the evidence, both negative and positive, that nervous tissue cannot be seriously damaged by either functional poisons or by the causes of functional neuroses. The negative evidence is, that however great the effects of a functional poison be, yet in no long time these effects pass off altogether, leaving the nervous system the same that it was before, in its function quite as much as in its structure. The whole question would be altered if the functions did not recover so perfectly. And this experience may be renewed over and over again with the same result. But want of any effect, either functional or structural, after such repeated experience, certainly implies no structural defect, for of what imaginable kind of structural damage can such a phenomenon be predicated? The positive evidence is, that the temporary character

of the severest symptoms of functional poison indicates that this severity cannot be due to processes which correspond in any way with organic changes when they produce severe results. The profound coma which the surgeon induces by his anæsthetic for just as long as he wills, and then intermits it, can scarcely own the same mechanism as the coma induced by a cerebral lesion. The only thing which they have in common is the final result, coma; but the processes by which the coma is induced must be essentially distinct in each case.

On the other hand, these correspondences between the action of functional poisons and the phenomena of functional diseases are not without their analogues in the phenomena of some diseased states, which depend upon the presence in the blood of known poisons which have been generated in the system itself. Thus I have had occasion to note in some patients the close resemblance between gouty asthma and common asthma, the attack coming on as unexpectedly in the night in the one case as in the other. Gouty headache is often indistinguishable from migraine, and likewise other gouty neuralgic affections, which, though caused by the constant, or at least frequent, presence of this blood poison, are nevertheless as intermittent as any of the so-called functional neuralgias. In one patient of mine the symptoms were occasionally those of true hysteria. The physician, indeed, may have no history of antecedent gout to suggest the true causation, and in several instances I have been led to a correct diagnosis by the high tension pulse alone. I need but mention also the frequency with which the symptoms of uræmic poisoning develop as suddenly in functional nervous manifestations as any functional neurosis does. As a rule, auto-infection by these recognized poisons shows the difference between their slow accumulation and the single introduction of a functional poison by various derangements in other organs; but their nervous developments are often as explosive, so to speak, as an attack of idiopathic epilepsy, so that if we were unaware of the coexistence of blood-poisoning we would rest content with such a diagnosis.

All these considerations, however, if we had to stop with them, would have the great disadvantage of appearing to be more or less speculative, and the profession is justly growing impatient of mere views on any medical subject. Modern organic chemistry, however,

is coming forward with certain demonstrated facts which must challenge the attention of practical physicians, though they may seem to involve the extension of the subject of auto-infection to the whole series of functional neuroses. The mere extension itself does not constitute an objection, for the modern subject of the relation of microörganisms to disease has been wider and more far-reaching than any such hypothesis would be. It is doubtful if the first advocates of the parasitic nature of communicable diseases would not have felt shaken in their conclusions if they had been told that their principles involved the admission that tuberculosis, and perhaps even cancer, not to mention pyæmia and malaria, were all due to microscopic forms of life. Now, when chemistry appears as if it would rival the microscope in its explanation of the problems of disease, it is natural that its claims should be received by many with the same incredulity which marked the first reception of the inferences of the bacteriologist. But just as the microscope tells us that we live and move in such an ocean of life that our one thin protective barrier of the skin should not be punctured, even by a needle, without every precaution against so introducing some unseen but living enemy, so does modern chemistry tell us that in the healthiest processes of our digestion a whole series of poisons is elaborated which are of the same nature as the functional poisons with which we have been long familiar, and which are quite sufficient to cause every variety of functional nervous derangements, and even to kill, without microscope or scalpel being able to tell why.

But between omnipresent microörganisms without, and unceasingly formed poisons within, we need not wonder that some medical minds ask how we live at all, and whether our doctrines do not prove altogether too much. Hence the width of the subject warns me that the time limits of this paper will only allow a mere reference to some of the researches which bear upon our topic. The decisive demonstration of the part which natural chemistry, so to speak, has in forming alkaloidal bodies will be found in Brieger's investigations on the formation of indol, which he showed to be generated by specific bacteria out of the products of pancreatic digestion, and then sent to the kidneys to excrete as indican. Conjoined with this we may mention the researches of Thudichum on the source of the coloring principles of the urine, as formed first in the intestine and then sent to

the kidneys for excretion. The pale urine of chronic Bright's disease would thus be a sign of one danger to the nervous system of auto-infection from this source, quite irrespective of the elimination of urea. But not only are such substances demonstrated to enter the blood along with its food-supply, but new light has been thrown upon the whole series of alkaloidal bodies as owning much more than one source of derivation. As Dr. Lauder Brunton remarks:

"We may now, indeed, regard alkaloids as products of albuminous decomposition, whether their precursor be contained in the cells of plants, or whether the albuminous substances undergo decomposition outside or inside the animal body, or by processes of digestion. Thus the poisonous alkaloid muscarine, which had only been known as obtainable from a plant, the *Agaricus muscaricus*, has been discovered by Brieger to be a product of the decomposition of fish. A considerable production of alkaloids takes place in the intestines, both when the digestive processes are normal, and more especially when they are disordered. At the same time alkoloids are being formed in the muscles and possibly in other tissues, and were all the alkaloids to be retained in the body, even only those formed in the intestine of a healthy man in twenty-four hours, they would be sufficient to kill him."

In illustration of these remarks of Dr. Brunton, we will only refer to some researches in the three allied poisons, choline, neurine, and muscarine. Choline, which has been found by Brieger to be a very common product of putrefaction, has been found by Boehm, Schaff, H. Gowers, Jahns, and others extensively in leguminous plants, as beans and lentils, in peanuts, cottonseed, hops, and therefore in beer, besides in various edible fungi. By a single substitution of a molecule of water choline is turned into the extremely poisonous substance neurine, a poison formerly stated by Liebreich as found only in brain matter, but Professor Schmidt has shown that when hydrochloride of choline is allowed to stay in contact with blood at the normal temperature it is converted into neurine; while Wurz has shown how choline by treatment with an acid in converted into muscarine.

The researches also on the elements to which the toxicity of normal urine is due, more especially by French investigators, are very suggestive, although, from the comparative infancy of this branch of science, many of the statements cannot be accepted without some reserve. Thus Bouchard shows that if the day be divided into three periods of eight hours each, the proportional quantities of poisons

excreted are: asleep, 3; early waking period, 7; late waking period, 5. The urine after sleeping and waking hours also differs qualitatively as well as quantitatively. The alkaloid of the urine of sleep is *convulsive*, that of the waking urine narcotic. Fasting increases the toxicity of the urine, while labor and increased respiration greatly diminish it. We would by such facts seem to have some clue to the nocturnal character of some cases of epilepsy, also of attacks of asthma, gout, etc., during the later hours of the night. One of the most significant results, however, of researches on this subject, on account of its bearing on the important subject of diet in functional nervous diseases, is the experiments by Chevrin and Roger, who found that the urine of a man fed exclusively on a milk diet lost the toxic properties of normal urine when injected into rabbits, guinea-pigs, and dogs indifferently, in the great proportion of one to ten.

We must leave this subject, therefore, with this patent conclusion, viz., that these facts at least afford a strong presumption that the living body is itself constantly producing agents which are quite capable of occasioning, under certain easily conceivable conditions, every symptom of functional neurosis. Headache, muscular languor, diarrhœa, depression of the heart or palpitation, depression of the spirits, and convulsions are among their toxic symptoms; and, moreover, like our familiar drug poisons, these body-generated alkaloids have their respective affinities for different nerve functions, as special and as characteristic as any of the agents of our materia medica. In fact, so close is their resemblance that they have become the stock material for puzzling juries in medico-legal cases, some of the animal alkaloids resembling conine, others nicotine, strychnine, veratrine, digitaline, atropine, etc.

Of course, against the perils of auto-infection, the system is provided with a variety of safeguards. One of the most efficient seems to be the antiseptic properties of the digestive secretions themselves, always in health-keeping putrefactive processes in the alimentary canal, in check. But the complex chemistry of these secretions is liable to numerous disturbing influences, notable among which are nervous irritations, especially those proceeding from the pelvic region, as is witnessed in the disorders of menstruation, or of pregnancy, in chlorosis, etc. I have thus long acted on this neuro-chemical

hypothesis in the treatment of hysteria. Another preservative function against auto-infection is well known as subserved by the liver. But this also seems very susceptible to nervous influences. There still remains a wide field, but little explored or known, of the resistance of blood elements themselves to the action of poisons. The whole question of immunity is now at the front of medical discussion and investigation, and is evidently as much a question of chemistry as of bacteriology. But it is in just this connection that a very probable clue is afforded to the phenomenon of intermittency in functional neuroses. If nervous influences are capable of deranging the chemistry of the body, why may not such perturbances of nervous origin, occurring now and then, as nervous actions characteristically do, suffice to produce either increased amounts of alkaloidal poisons, or else to diminish the effectiveness of the normal antidotal processes? We have many positive indications that the chemistry of the secretions can be materially affected by nervous impressions. One of the oldest known instances of this kind is the ready production of alkalinity of the urine in conditions of nervous depression or exhaustion, and along with that presumably the interference with the acidity of the gastric juice. Now, the latest observations point to the acidity of the gastric juice as the chief factor in the germicidal power of the stomach secretions, and thus we have another explanation why a bath should not be taken on a full stomach, as it has long been known that the immersion of the body, even in an acid bath, promptly causes alkalinity of the secretions, as shown by its effect on the urine.

While these considerations, therefore, seem to offer us a hint of the explanation of intermittency in functional neuroses, they do not militate against the toxic origin of certain functional nervous diseases which are not intermittent but rather continuous. For it is easy to see that the generation of some animal poisons, or the antidotal processes against the same, in some cases may be permanently as well as intermittingly affected, so as to allow of a more or less constant condition of specific auto-infection. Some years ago I cured a patient of Basedow's or Graves's disease, by putting her upon an exclusive diet of fermented milk, after having vainly tried to arrest the disease by all the remedies then reputed to be of service in this affection. After some months of disappearance of the morbid symptoms she

resumed ordinary diet, and ere long the disease returned. She then resumed the milk (fermented) diet with the same good effect as before, to have the disease return when she abandoned the milk again. This experience was repeated three times, and that one case has taught me ever since to treat all cases of rapid heart action without fever and with symptoms of gastro-intestinal derangement as cases of this disease, whether there was exophthalmus and thyroid enlargement or not, and, as primarily cases of auto-infection, and to treat them with appropriate diet and with intestinal antiseptics, with results which very favorably contrast with my former experience in this complaint.

I need only refer here also to the admirable investigations of Dr. W. Hunter on the causation of pernicious anæmia as due most likely to the presence in the portal circulation of an intestinal ptomaine. During my last service at the Roosevelt Hospital I treated a case of this affection, which had previously taken arsenic without appreciable benefit, by free doses of salol, soda benzoate and bismuth salicylate, and β-naphthol, with apparently very favorable results in checking the fever and improving the blood.

It may be urged that the toxic theory of functional neuroses can hardly hold good for those cases of epilepsy in which an intra-cranial organic focal irritation is manifestly the occasion of the fits, as in traumatic epilepsy or other form of pachymeningitis. This objection reminds me of the objection to the bacterial origin of tuberculosis, because it was supposed that phthisis must be primarily due to a fault of nutrition, on account of the disease being so markedly hereditary in certain families. Such objections are based upon a too exclusive estimation of the etiology of disease. We now know that scarcely any infection has only one factor required for its development, and that, in addition to the specific virus, we must have an individual susceptibility for its infection, and that susceptibility can very well be hereditary. So in traumatic epilepsy, something else than the presence of the permanent organic source of irritation must account for the intermittent epilepsy, for the permanent irritation cannot itself be enough to cause the convulsion, else the convulsion would neither intermit nor cease, but be as continuous as the irritant is. Conversely, on this hypothesis, every such organic irritant should cause epilepsy, whereas it does so only in a minority of cases of the kind, pachymeningitis and traumatism occurring in a

multitude of instances without any consecutive epilepsy. All that we can say of these cases, as well as those who present congenital malformations of the skull or other stigmata of degeneration, is that the effect of these organic defects is to lower the resistance of the cortical centres to the causes of functional derangements, and nothing more. In conclusion, we would briefly point out the important bearing of that view of functional neuroses on treatment as follows:

1st. Instead of vaguely expecting help from structural anatomy, to show us the pathology and then the treatment of this difficult class of diseases, and meanwhile choosing our remedies according to the old empirical method, the physician should look for aid to advancement in the knowledge of the chemistry of diet. Something has been done in this direction, but we are yet far from completeness in the estimation of the intermediate as well as the ultimate destination of the proximate principles of our food, or of the specific perversions of their digestion, or of the particular relations of such perversions to functional nervous disturbances. Enough we do know, however, to cause the practitioner carefully to investigate in every case of epilepsy, for example, any perversions of gastro-intestinal function, or of secondary assimilation, or of excretion. Family histories of such perversions are then of especial importance to take into account.

2d. Gastro-intestinal antisepsis should be studied as a particular branch of therapeutics. The value of a certain class of purgatives, conjoined with the administration of antiseptics, has been particularly impressed on my mind in the treatment of migraine, of hysteria, and of melancholia with quickened pulse.

Lastly. The investigation of leucomaines, of which lithæmic states are an example, is of equal importance in a great variety of morbid states, with functional disturbances. Directed by these three principles, suggested by the progress of organic chemistry, I think that our treatment of functional diseases will be much more effective than if we continued to seek for more drugs with specific properties or fruitlessly to await the verdict of pathological anatomy.

MALARIAL HÆMATURIA OR HÆMOGLOBINURIA, AND THE VALUE OF QUININE IN THE AFFECTION.

By H. A. HARE, M.D.

Bloody urine occurring in persons who have been exposed to malarial influences is a symptom which has only attracted general attention for the past forty years. I have used the rather uncouth term "bloody urine" because much discussion has taken place as to whether the renal secretion at such times is discolored through the presence of hæmoglobin or blood itself with the corpuscular elements. I cannot in this paper discuss this question to any extent, because it would be out of place; yet I am aware that the point is important, since much depends upon the determination of the facts. Suffice it to state that very considerable research in the literature of bloody urine in association with malaria shows that both conditions exist at certain times in certain cases, and we must conclude that both hæmoglobinuria and hæmaturia may be present in this condition.

Soon after the appearance of the first edition of my book on therapeutics I received a number of letters from well-known physicians in the South criticising a statement which the book contained, namely, that quinine was useful in malarial bloody urine, and this directed my attention to the subject of which I speak to-day. An examination of the literature at my command showed that very positive opinions pro and con were generally held, and I determined to solve, if possible, what I believed to be a contradictory condition of therapeutics, which might be cleared up if only all sides of the case could be brought forward. To this end I sent out six hundred sets of the following questions to physicians residing in the areas marked in the census as having a death-rate from malaria of seventy per thousand or over:

Is hæmaturia or hæmoglobinuria a frequent complication of malarial disease in your locality?

Do you regard hæmaturia as a dangerous complication?

When this complication occurs does it appear during the malarial paroxysm?

If not during the paroxysm, when does it appear?

Is it most common in males or females?

At what age is it most common?

Do you regard *quinine* as a *harmful* or *useful* drug during the existence of malarial hæmaturia or hæmoglobinuria?

Have you ever seen quinine *produce* hæmaturia or hæmoglobinuria in a person suffering from malarial disease?

Have you ever seen quinine *cure* hæmaturia or hæmoglobinuria in a person suffering from malarial disease?

To these questions I received one hundred and ninety-three replies, of which I could utilize one hundred and fifty-four.

The first question was placed in order to give me some idea of the actual experience of my correspondent. The second to determine whether his cases were of a severe type with a high mortality, because the force and severity of the disease must seriously modify his ideas concerning it. The third question is important in order that I might obtain facts relating to the effect of the chill on the production of the hemorrhagic condition, and the fourth obtains still further information of this character. The fifth and sixth determine the interesting points of sex and age. The remaining questions are all devoted solely to the treatment.

The returns may be divided into two classes—those coming from physicians who state that the disease is common in their practice and those in which it rarely occurs. Fifty-four of the 155 see it frequently, and of these 4 are in Alabama, 9 in Georgia, 14 in Mississippi, and 27 in Texas.

That the symptom of hæmaturia in malarial disease is a most dangerous one is shown by the following table:

	Experienced.			Inexperienced.		
	Dangerous.	Not dangerous.	Uncertain.	Dangerous.	Not dangerous.	Uncertain.
Texas	24	2	1	42	4	...
Mississippi	14	...	...	29	...	...
Georgia	9	...	...	14	...	...
Alabama	4	...	...	9	...	2
Total	51	2	1	94	4	2

In 642 cases collected by Jerome Cochran, Health Officer of Alabama, from different practitioners, there were 158 deaths, the death-rate being about 25 per cent.

It is interesting to note in passing that males are much more frequently afflicted than females, probably due to greater exposure.

Dr. T. W. Ayres, of Jacksonville, Alabama, calls my attention to the fact that the Report of the State Board of Health of Alabama shows that in 1887, 1888, and 1889 there were 39 deaths from malarial hæmaturia, of which 25 were males and 14 females. And he also records that of 108 cases 73 were males and 35 females:

	Experienced.			Inexperienced.		
	Males.	Females.	Equal.	Males.	Females.	Equal.
Texas	25	...	3	35	3	4
Mississippi	12	1	1	15	4	4
Georgia	6	2	1	8	...	4
Alabama	4	...	...	11	...	...
Total	47	3	5	69	7	12

Persons from the age of ten to forty-five are most often attacked, perhaps for similar reasons.

The results reached in some respects are very satisfactory, but those bearing on the usefulness of quinine are not so, and apparently leave the subject in as chaotic a condition as before; yet I hope to show that something has been done toward clearing up a hitherto unexplained therapeutic contradiction, for it is evident that in a disease so prevalent, so dangerous, and so interesting there must be some cause for the widely differing opinions held by the best men in the South. (See following table.)

	Experienced.				Inexperienced.			
	Useful.	Harmful.	Cure.	Produce.	Useful.	Harmful.	Cure.	Produce.
Texas	11	10	5	12	22	20	15	9
Mississippi	5	6	3	7	13	14	10	7
Georgia	3	6	3	6	6	6	4	5
Alabama	...	4	1	2	7	3	...	...
Total	19	28	12	27	49	43	29	21

At the very outset it is necessary to remember that the bloody urine is a symptom, not a disease, and while it seems unnecessary to

recall this fact, a close study of many of the papers shows that it has not been regarded symptomologically.

The recollection of the fact that bloody urine is but a symptom at once does a great deal toward clearing up much apparent contradiction in regard to the pathology and treatment of the condition, since we are now able to recognize the important fact that malarial disease may result in bloody urine in a number of ways, and that very different varieties of malarial poisoning may cause the trouble.

In the first place, there are many cases recorded in the literature of the subject in which bloody urine has come on with the first malarial paroxysm of the intermittent type which the patient has ever had and at a time when the history of the case renders it certain that a hidden malarial condition could not have previously damaged the renal tissues or those of other organs in the body. In other words, there are cases in which a free hemorrhage from the kidney takes place by reason of the chill in much the same manner in which hemorrhage takes place in acute nephritis due to exposure to cold or to irritants. Under these circumstances there may or may not be developed a true organic lesion of the kidney in the sense of permanent disease.

Secondly, we have cases in which bloody urine appears, not in the first malarial paroxysm of the intermittent type, but in association with the later attacks, which may have followed the first rapidly or slowly. In these cases there may be no further cause for the hemorrhage than excessive congestion, but in all probability the vast majority of cases present distinct renal changes which permit such a symptom to develop when the paroxysm asserts itself. That changes of the renal tissues do take place is a fact so generally accepted as to need no further comment; and should such evidence be desired, the very able paper of Dr. Atkinson, of Baltimore, need only be referred to.

The Tri-State Medical Society Committee of Alabama, Tennessee, and Mississippi have found nephritis in all fatal cases of malarial hæmaturia. Ralfe states that renal changes undoubtedly occur, although in some instances these may be due to cold and damp rather than the malarial poison; and Atkinson has shown that malarial nephritis is tubal and diffuse, and that the inflammation is most marked in the neighborhood of the glomeruli. Kiener and Kelsch

also describe a hæmoglobinuric hyperæmia as occurring in an acute attack of ague in which the organs were intensely congested. The cortex is cloudy from blood coloration, the glomeruli are prominent and red and the pyramids redder still. The results obtained from my correspondents show that the bloody urine nearly always comes on with the paroxysm of malarial disease.

	Experienced.			Inexperienced.		
	During.	After.	At any time.	During.	After.	At any time.
Texas . . .	13	5	7	36	6	4
Mississippi . .	10	3	1	19	4	3
Georgia . . .	5	3	1	5	6	...
Alabama . . .	4	...	...	6	3	1
Total . . .	32	11	9	66	19	8

Thirdly, we pass from these cases of bloody urine due to intermittent forms of malarial disease to those due to the remittent forms, which in many cases have gradually merged from the first to the second. In these patients the process by which we have developed a bloody-colored urine may be very complicated, since it may be due to renal incompetence, functional or organic, or to a true hæmoglobinuria arising from dissolution of the red blood-cells in the blood-vessels or blood-making organs. Finally, we must remember that all the blood elements may be simultaneously present, and that the opacity of the urine may be in large part due to bile-coloring matters which in one sense are derived from the same source, namely, disorganized corpuscles. In these cases the malarial disease has produced renal and vascular changes in a number of ways. In the first place, the frequent engorgement of the kidneys has weakened the vessels of these organs; in the second place, the recurring malarial attacks have forced the kidneys to eliminate effete matter of a physiological character in greatly increased amount at the same time that the poisonous products of high fever, disordered digestion, and of the disease itself have to be discharged from the blood.

Again, the clinical and pathological picture of the remittent forms of malarial hæmaturia shows that the spleen and liver, and even the entire vascular system, is impoverished under these circumstances. The liver is enlarged, congested, and filled with quantities of broken-down blood, and the gall-bladder is filled to bursting with bile. The

structure is softened and broken down until only the word pulpy describes the structure of the parenchyma of the organ. The spleen is found in a state as closely resembling the liver as it is possible for one diseased organ to resemble another, and we have before us an organism which of necessity must tend to present hæmoglobinuric or hemorrhagic manifestations. The two organs which manufacture and destroy blood-cells are diseased and inoperative, and the excretive power of the liver is in abeyance, as is seen by the engorged gall-bladder. The biliary coloring-matters are imperfectly prepared from the broken-down corpuscles, and we have all the opportunities for both hepatogenous and hæmatogenous jaundice—a symptom, by the bye, of the greatest constancy in severe hemorrhagic malarial fever. There is scarcely an author or note-taker who does not insist on the jaundice being one of the most noticeable features of the severer forms of the disease.

These cases may be of all degrees of severity, from the mildest, such as are discussed by Bemiss in Pepper's *System of Medicine*, to the malignant cases seen by our Southern physicians, which have been mistaken for yellow fever or called black hemorrhagic jaundice.

Bemiss states that he has again and again shown the influence of these various destructive factors which I have named by producing on the arm of a malarial patient exaggerated extravasations of blood by gentle suction; and he goes on to point out that hemorrhages in malarial fevers are never general, but only appear from those surfaces which are seats of congestion during the cold stage of an intermittent.

The very presence of bile acids in the bloodvessels also tends to produce a hæmatogenous jaundice, for, as Harley points out, bile acids have a peculiarly disintegrating effect on the red blood-corpuscles. Harley suggests this factor as being the chief cause of the hæmoglobinuria at such times, and the hypodermatic injection of bile acids in the lower animals results at once in hæmoglobinuria precisely like that seen in man in malarial attacks of a moderate type. The same authority also believes that the condition referred to is in great part due to the action of the malarial poison on the liver.

Before leaving this group of cases it may not be out of place to impress the fact that in the severe forms of hemorrhagic malarial fever there is frequently developed, in addition to the jaundice and

hemorrhages, dark, bilious purging and in some instances uræmic coma and convulsions.

The fourth class of cases to which we must direct our attention is that in which bloody urine appears indirectly malarial or entirely free from malarial influences. This condition is sometimes called paroxysmal hæmoglobinuria, although it is distinct from that due to any parasite. That is to say, the mere chilling of the surface may cause in susceptible persons a hæmoglobinuria similar to that caused in such individuals by immersing the hands in iced water, and this condition may be produced either by exposure to cold and damp, which are generally present in malarial localities, or to the chill of the milder forms of malarial paroxysm. This class is closely allied to or identical with that mentioned by Harley, who points out that the characteristic of one form of malarial hæmoglobinuria is its intermission, the urine being at one hour limpid, the next hour bloody, and the third clear again. The possibility of confusing the hæmoglobinuria of idiosyncrasy just described, when in a severe form, with true and severe malarial poisoning is very great. The entire history of paroxysmal hæmoglobinuria teems with reports of cases in which the chief manifestations of a malarial attack were present, such as chills, fever, and sweats. Lichtheim and Ponfick have shown that the injection of lamb's blood into the vessels of man results in violent shivering, fever, sweats, and pain in the lumbar region over the kidneys.

Finally, we find that there may be a fifth form of bloody urine occurring in malarial regions independent of malarial influences, namely, that described by Bohn, who has described a form lacking in periodicity. It occurs also in non-malarial neighborhoods and particularly affects negroes, whereas malarial hæmaturia does not affect this class, as a rule.

While the various forms of bloody urine may be divided into classes in the way in which I have done, it is important to remember that such a division is largely artificial, and that each group may shade off into the next. Thus the rapid changes in the appearance of the urine in the mild forms described by Harley are represented in the severe forms of remittent disease, according to Michel, by distinct remissions in the discolorations of the skin, the color of the

urine, and the general symptoms, although these remissions may last but a short time.

Turning now to the treatment of the conditions under discussion, we come to a most important portion of the subject. This is the more difficult because it is evident at the beginning that the variations of treatment must be dependent upon the variations of each individual case. It is impossible for the writer to say positively that quinine or other remedies shall or shall not be used in every case. The whole story of each case is necessary before any opinion for or against the quinine can be given. On the one hand, we are assailed by the undeniable fact that quinine is a specific for the malarial disease producing the bloody urine; and yet it must be evident that the conditions present are often very distinct contra-indications in themselves to the use of quinine.

Taking up for therapeutic consideration that form of bloody urine which is associated with the first paroxysm of intermittent fever and joining it with that in which the bloody urine follows after a number of consecutive attacks, let us balance the advantages and disadvantages of quinine. We have in such kidneys a condition of engorgement and congestion and true inflammation, and there is commonly in association with this irritability of the genito-urinary tract. All writers of experience state that quinine, particularly in full doses, possesses distinct irritative effects on this tract, and I have proved that in poisoning by quinine the kidneys become congested and finally inflamed.

Guyochin[1] has reported cases of genito-urinary irritation after the use of quinine, and Faginoti reports a case in which there was pain in the urinary passages and the discharge of a few drops of blood on urination. Monneret has seen positive hæmaturia follow its use, and Rivet[2] has observed vesical spasm and hæmaturia after an ordinary dose of the drug. Dasset[3] reports the development of hæmaturia, with retention of urine, from cystic irritation due to quinine, and Cachere[4] records two cases in which hæmaturia followed the use of quinine. In one of these a boy of thirteen had profuse hæmaturia

[1] Action Physiol. et Thérap. de la Quinine, Paris, 1872.
[2] Rivet, L'Union Médical, November 1, 1884.
[3] Bulletin de Thérapeutique, xv, 248.
[4] New Orleans Journ. of Med., October, 1869.

after the dose of ten grains, and a girl of seven years was affected similarly whenever quinine was used.

These may represent the instances reported by my correspondents of cases where quinine produced malarial hæmaturia, and this is more likely in view of the studies of Karamitsas, Pampoukis, and Chomatianos, about to be quoted, and of the statement of Stillé that quinine irritates the urinary organs, and that if any part of this tract is diseased the disease is aggravated.

In these two milder forms of bloody urine there is rarely great danger during the malarial paroxysm, and it would seem well to withhold quinine, if this can possibly be done, until the kidneys have had time to rid themselves of the congestion and blood which are in their tubules. To give quinine after the bloody urine has been produced by the chill is equivalent to "shutting the door after the horse is stolen."

All writers of experience state that in intermittent fever the old adage, "an ounce of prevention is worth a pound of cure," is true, and logically quinine would really only be of service in malarial hæmaturia, provided its effects are felt before the paroxysm occurs, for it is during the first stage, or that of chill, that the engorgement of the kidney takes place.

The stage of fever and sweating having come on, the case can be treated by remedies not directly antimalarial, yet all directed to the relief of the symptoms, and it is manifest that hæmaturia once being developed quinine cannot act as a hæmostatic, whereas aromatic sulphuric acid or other astringents or ergot may do so. The only reason for using quinine at this time would be to prevent the rapidly recurring attacks. Similarly, we use bromide of potassium to prevent epileptic attacks, and an attack once present we give no more during the period of coma unless we have reason to believe that other attacks may rapidly follow, when we temporarily increase the coma by the use of the cerebral sedative. Quinine is contra-indicated at this time for the reason that it will almost certainly increase the renal difficulty and predispose to future attacks of hæmaturia by irritating the kidneys. That this belief is not theoretical is shown by a large amount of clinical experience.

The attack can be treated by chloroform spirit, by heat in the cold

stage or cold in the hot stage, and by all the remedies commonly employed in treating malarial attacks, other than quinine.

In hæmoglobinuria occurring with the paroxysm there is probably less danger in using quinine than when true hæmaturia is present, since the kidneys are not as hindered and clogged by blood-clots; but even here it must be evident that quinine can only stop future attacks, not the one already in existence. Should the attack of hæmoglobinuria be prolonged, indicating that the malarial poison is destroying the corpuscles independent of the chills, then quinine may be needed. If it is given, I believe that cholagogues, followed by a brisk purge, should be used to aid in the elimination of coloring-matter through the liver and bowel and to relieve the kidneys of all labor which it is possible to remove. If in any case the intermittent paroxysms are so frequent as to make the quinine necessary, in view of the fact that other measures have failed, the same attention to the bowels should be given; the kidneys flushed out by diuretics, such as the vegetable salts or potassium, and the quinine given because the danger of the continued attacks is greater than that of renal involvement from the drug.

The third class of cases, namely, those which are included under the severe forms of bloody urine associated with jaundice and general hemorrhages from the stomach, the bowels, and the nose, are more difficult to treat than those just discussed. They present all the difficulties which non-hemorrhagic remittents produce and the peculiar inability on the part of the absorbents, coupled with the bilious vomiting, make all medication difficult, let alone the complication of bloody urine. Much that has been said in regard to the condition of the kidneys and the contra-indications to quinine in the milder forms already spoken of holds with the severe form of hæmaturic fevers now discussed, yet the very severity of the condition calls for quinine, although the contra-indications are stronger than ever. This may be cleared up, however, by a recollection of three facts, namely, that this malignant form comes on suddenly with the access of a malarial attack in a patient already broken down, and as an attack of hæmaturic jaundice without any evidence of another dose of malarial poison; third, there are a number of remedies which are capable of doing much good before quinine is resorted to. The quinine will be needed in the cases suffering from active malarial paroxysms

imposed on the subacute or chronic forms, but will not be needed in the second class of chronic cases, who should be treated by other measures directed to the relief of the dyscrasia and bloody urine.

The next point of interest is as to the use of cholagogues in the severe forms of the disease.

In regard to whether we shall precede the quinine, when we use it, by cholagogues there seems to be at first glance some dispute, which in reality rests upon the methods employed in their administration. Norcom and others have protested vehemently and correctly against an attempt to produce a mercurial effect on the entire system, and McLean goes even further than this and declares against the use of calomel in bilious remittents, thinking it absolutely harmful. Norcom admits the value of purgation, provided it can be obtained without exhaustion.

On the other hand, a very large majority of the profession, as far as I can learn, give calomel or podophyllin to increase the effect of quinine, and declare that the purgative effect obtained is of great value, even when the quinine is given hypodermically and so does not have to be absorbed by the stomach. The cholagogue, if given at all, should be in active dose if podophyllin is used, and if calomel is given should be promptly followed by saline purges in small doses, so as to avoid vomiting and to prevent the absorption of the drug and its depressant influences upon the system, already depressed and in a condition of degenerative change.

The question as to whether the quinine produces a cessation of the hæmaturia is one which it is impossible to answer positively. It certainly only does good if the case is one of those where the malarial influence is pernicious, and then it acts solely by shortening the general attack without directly checking the hæmaturia.

The very important question as to whether quinine produces hæmaturia, as independent of malarial influence, has already been discussed and answered affirmatively, and it seems to be an undeniable fact that in some persons quinine possesses very distinct hemorrhagic tendencies.

This hemorrhagic tendency may also extend itself to the lungs, for Gauchet[1] has seen hæmoptysis, and Simon de Ronchard[2] saw

[1] Thérap de la Quinine, Paris, 1872.

[2] Gazette des Hôp., Janvier, 1861.

several such cases after the use of eight grains of quinine a day, the lungs and heart being healthy. A stoppage of the quinine was followed by a stoppage of the hemorrhage and a renewal by a renewal. Lewin[1] states that Merat has found quinine in the bronchial mucous membrane after its administration. An interesting case is quoted by Stillé from Gelineau of a delicate woman who took ten grains of the sulphate of quinine on an empty stomach, and who was attacked in about two hours with rigors and cold sweats. The face was pale, eyes sunken, the pupils dilated, the teeth clenched, the limbs were stiff, and there was a bloody discharge from the vagina, although menstruation was not at hand. In this case all the symptoms pointing to malarial poisoning were produced, and it might have been called by a careless physician malarial hæmaturia.

Malarial fevers also distinctly predispose some persons to this action of quinine, and the literature of Greek and French writers is particularly prolific in this class of cases. Probably the most thorough paper on this subject is that of Karamitsas, of Athens, who has observed with the greatest care no less than seven cases of quinine hæmaturia, one female child and six men, and reports several other cases reported personally to him. His paper, which is of the greatest possible interest and value, was published in the *Bulletin Générale de Thérapeutique*. At least two of his patients were physicians or medical students, and he was able again and again to produce hæmaturia in these persons by giving quinine, although it had been months and years since they had any malarial attacks. Not only was this the case, but in all cases they had failed to have hæmaturia in any of the malarial attacks, except in those in which quinine had been used, in which case the hæmaturia at once came on. By means of careful control experiments this was repeatedly proved to be the case, and the only relief obtained from the disease was by voyages, baths, and arsenic.

A very interesting point made by Karamitsas is that in all his cases, while quinine had this effect, they had at some previous time had more or less malarial disease, and that he has never seen quinine hæmaturia except in cases at one time malarial. In his cases, however, the quinine caused hæmaturia not only during the attack, but forever after, even when the case was in perfect health.

[1] Untoward Effects of Drugs.

It appears, moreover, that the use of quinine can sometimes occasion a bilious hæmaturic fever. He learned this fact for the first time from a quartan fever patient, who asserted that every time after taking quinine he was attacked by fever, with hæmaturia and jaundice. For this reason he urgently begged Karamitsas not to prescribe quinine for him, as other physicians had done who would not believe his statements.[1] Karamitsas also has seen a little girl of nine years who succumbed to the consequences of a bilious hæmaturic quinine fever. Her father, who was a physician, said that every time his daughter took quinine she was affected with a slight bilious hæmaturic fever; but as since the last attack considerable time had elapsed, urged by a confrère, he gave her quinine, after which the fatal fever came on. M. Rizopouloo after giving quinine has seen a bilious hæmaturia produced.

The following case, reported by Karamitsas, also shows that hæmaturia may be produced in an attack, otherwise non-hæmaturic, by the use of quinine:

The patient, after eating irregular meals, arose October 14th with much anxiety, a headache, and slight lumbago, but without fever. Two hours after noon some fever came on with slight chills. The temperature rose toward evening to 38° C., the pulse toward 100; the tongue was a little dry and covered with a white coating. There was thirst, heaviness in epigastrium, headache, especially in the frontal region, and anxiety. They gave him soda-lemonade. About two hours after midnight the fever diminished; the temperature became 37.5°, but the other symptoms remained the same. In the morning (October 15th), as the patient had had no evacuation for two days, he was given a decoction of tamarinds with manna, which was followed by evacuations. The temperature toward noon was at 37°. Except for extreme lassitude the patient felt no other discomfort. Three hours after noon came a fever without chills, more severe than the day before. The temperature rose little by little to 39.5°. Insomnia and fever persisted through the entire night. About three hours after midnight the temperature descended to 38°; then the patient began to take quinine; he took, up to 7 o'clock in the morning, 20 grains—5 grains an hour; an hour after the first dose he felt much weakness, heaviness, with pains in the lumbar region, and a desire to urinate; he passed, shortly after, a copious amount of urine of a red-black color, although during the paroxysm and before having taken the quinine there was only ordinary febrile urine.

[1] Tomaselli has also seen cases of long-continued malarial intermittent result in producing a condition in which quinine would bring on attacks of bilious hæmaturic fever.

The weakness became still greater, also the painful heaviness in the lumbar region. Two hours after having taken the last dose of quinine he again passed bloody urine. For twenty-four hours his urine always presented a red color, but little by little it became lighter and less bloody, and on the morning of October 17th had a normal color. The patient felt no indisposition save weakness; he was very pale, and his conjunctiva during two days was of a yellowish color, which disappeared little by little.

A type of hæmoglobinuria caused by quinine has been written of by Du Chassaing, in Guadeloupe, and by other physicians in France and Italy.

It has been found by these writers that the manifestations of hæmoglobinuria after the use of quinine depend upon a special predisposition to the drug or to an idiosyncrasy which affects members of the same family. Its appearance is very rapid after the administration of the medicament, but its duration and intensity is variable, according to the size of the dose and the degree of susceptibility of the patient.

In many respects the attacks are closely analogous to those seen in malarial poisoning, the urine having the peculiar color of methæmoglobin, which a spectroscopic examination shows to be present. All of the salts of quinine are capable of producing this symptom, the rapidity of the action being somewhat governed by the readiness with which they are absorbed, and it is a point worthy of notice that muscular fatigue, febrile reaction, or a chill are powerful adjuvants of this peculiar effect. The prognosis in general is favorable, and is never grave except after the administration of massive doses of quinine, when profound alterations may be found in the blood, and such an accumulation of methæmoglobin may take place that it is impossible for the kidneys to eliminate it or for the liver to act properly, and as a consequence of this there is danger of biliary intoxication consequent upon the primary symptoms.

Carreau, who writes on this subject, warns physicians against the reckless employment of quinine in its various forms without carefully examining the history of the patient in order to discover any idiosyncrasy, and recommends that, as the condition is perhaps due to a lack of alkalinity in the blood, it may be well to administer, before the quinine is given, full doses of bicarbonate of sodium. For the icterus, which is sometimes produced, recourse must be had to the oil

of turpentine and the general treatment which is employed in cases of severe jaundice.

Pampoukis and Chomatianos, of Athens, record a number of cases in which quinine caused hæmoglobinuria. They found that the sulphate was chiefly responsible for this, as the other salts did not have so positive an effect. Seven grains produced a hæmoglobinuria lasting twenty-four hours, and about a grain produced attacks lasting five to six hours. They believe that in some individuals quinine has the effect named and in others prevents hæmoglobinuria if malaria is the cause.

Finally, we come to the most important question of this entire paper, namely: Shall quinine be used in malarial hæmaturia or shall it not? I think it is evident from what I have said that in the presence of the milder forms of the disease it should not be employed during the hæmaturia nor in those cases in which idiosyncrasies exist.

In those cases which are malignant in their manifestations in other lines than the mere hæmaturia and depend on a malarial paroxysm superimposed on a malarial dyscrasia, then quinine is needed; but in that hæmaturia following prolonged subacute or chronic malarial poisoning quinine is not to be given in full doses, but only as a tonic, the physician relying upon change of climate, nutritive foods, tonics, and other drugs to renovate the patient's tissues. Of these drugs and their method of employment I hope to speak in a paper now in preparation.

DISCUSSION.

Dr. I. E. Atkinson: Dr. Hare's paper is so thorough and exhaustive that it is hardly to be discussed off-hand. I shall refer only to one or two points.

Undoubtedly the keynote has been struck, in regard to the production of hæmaturia and hæmoglobinuria by quinine, when it is attributed to idiosyncrasy. That quinine has any fixed tendency to produce hæmoglobinuria or hæmaturia I do not believe; that idiosyncrasy will call this condition forth I have no doubt. There is probably no drug in the whole materia medica that brings out expressions of idiosyncrasy more than cinchona bark, and we have in these a wide range of pathology. I can speak more of hæmaturia than of hæmoglobinuria. It has been my experience to come across many cases of malarial hæmaturia. It is true that my observations have been in

individuals who have come to me from the localities in which the hæmaturia has been acquired. Some five or six years ago it was my good fortune to be consulted by a patient suffering from persistent hæmaturia. He came from an extremely malarious region, in the Isle-of-Wight County, south of the James River, in Virginia. He was aware of other persons suffering as he was, and I had the opportunity of studying the cases of several of them. These persons, while living in a malarious country, did not necessarily suffer from distinct paroxysms of malarial fever. Their hæmaturia would come on at irregular times, would last for weeks or months, then would stop only to recur again. They were very anæmic. It occurred to me that these cases might be of parasitic origin, and my investigations were made with regard to determining this point; but, unfortunately, I was never able to verify my suspicions. I looked for the Bilharzia hæmatobia, but did not find it, nor did I find any parasite, but the suspicion was in my mind, and still remains there, that these forms of hæmaturia that are found in certain low portions of the country in which malaria prevails will be found to be due to some form of parasite not malarial. I have saturated these people with quinine without good results. I have stopped the hæmaturia by other agents, notably turpentine. One case, that of a physician, I saw three weeks ago looking very much better. He had had returns of his hæmaturia, but they became less and less intense, and he became better and less anæmic.

Dr. Loving: Did you find the filaria sanguinis hominis?

Dr. Atkinson: No; though it was looked for.

Dr. Loving: I do not know that it has ever been found in Virginia.

Dr. Tyson: With the mild form of malarial hæmaturia I have had some experience. To the more serious form of Southern hæmaturia I have also given some consideration, but have had but little personal contact with it.

With regard to the first form, such as occurs occasionally in the Middle States, sometimes ushered in with a chill, more frequently, perhaps, with a simple chilly feeling, or again with a blueness of the lips and the ends of the fingers and end of the nose, I am satisfied that for these cases quinine is the remedy. It does not matter very much how it is given, whether in small doses frequently repeated, or in larger doses as are most usually given in malaria. With the malignant hæmaturia of the South the conditions appear to be different. The mischief is already done when the hæmaturia sets in. The blood, through the action of the poison, whatever it may be, has been reduced to a broken-down condition, the plasma of the corpuscles has been so acted upon that it will no longer hold the hæmoglobin, or the bloodvessel walls have been so affected that they cannot retain corpuscles or hæmoglobin. As I have said, the mischief has already been done, or, as Dr. Hare puts it, "the horse has been stolen, and to give quinine at this stage is to shut the door." Hence, perhaps, the frequent failures with it in the far South.

There doubtless, however, occur all over the country, even in the extreme South where the malignant cases occur, certain of the milder forms, such as we have in the Middle States, in which quinine is equally efficient. This may account for the difference of opinion amongst southern physicians as to the effect of quinine. On the other hand, as a prophylactic it would seem that quinine is the proper remedy in districts where this disease is so prone to occur.

I have had some experience, also, with the class of cases mentioned by Dr. Atkinson. They have come, to the best of my recollection, from North Carolina, occasionally, perhaps, from Virginia, sometimes from Pennsylvania. In these there has been a persistent hæmaturia extending over weeks and even months without very seriously affecting the health of the patient. These I have treated precisely as he has treated them: I have saturated them with quinine and given them arsenic until they were œdematous, without any effect whatever. Most commonly this form of hæmaturia has been reached in my hands by the use of astringent mineral-waters, such, for example, as Rockbridge alum water, carrying out, in another way, the treatment of Dr. Didama referred to. I have in mind a medical man from the vicinity of Philadelphia who had this condition extending over a long period. He was treated by me with every remedy which occurred to me. He even went south to drink the waters of astringent mineral-springs. Finally he went to Clifton Springs, New York, where he improved. Precisely what the treatment that was practised upon him there I do not know. My idea is that it terminated spontaneously. He is living to-day, a hale, hearty man of eighty.

In studying these cases with the same object in view as had Dr. Atkinson, I was not led to the view that they were parasitic in origin. I never, at least, found evidence of the presence of a parasite. I would hardly have expected the improvement which always ultimately occurred if they had been due to a parasite.

In regard to the harmful effect of quinine in these severe cases, in increasing the hæmaturia, it seems to me that if I were living in the South and were confronted with such a case I would prefer to run the risk of using quinine. When quinine produces hæmaturia it must be the result of idiosyncrasy, and I would prefer to run the risk rather than lose the chance of the good it might do.

Dr. Stockton: Some years ago, at a meeting of the American Medical Association at Cincinnati, I remember that a paper was read on the subject of hæmaturia by Dr. Didama, of Syracuse, N. Y., in which he recounted a number of very severe cases which he had treated successfully by the abundant use of alum. I have had experience with it since that time, and I believe that many of the cases of hæmaturia that have resisted other remedies can be controlled by the use of alum in large doses. Dr. Didama used it in ten or fifteen grain doses each hour during the day, or when the patient was awake. I have given doses of this size until there was great diminution of the hæmaturia, and then in smaller doses. I saw no nausea.

Dr. Henry: Before concluding that quinine is injurious in any form of malarial poisoning, it should be thoroughly established that the cases in which its exhibition was followed by untoward symptoms were genuine examples of malarial fever. Both hæmaturia and hæmoglobinuria may be due to many other causes than malarial poisoning, and it is doubtful whether in the cases collected by Dr. Hare these non-malarial causes of the symptoms in question have been thoroughly excluded. Confining my attention to hæmoglobinuria, I would call attention to the fact that this symptom is but the expression of a state of hæmoglobinæmia; *i. e.*, a state in which the hæmoglobin is separated from the red corpuscles while the latter are in circulation. Now, there are many substances besides the malarial organism (the hæmatozoon malariæ) which will effect this separation. For example, the inunction of pyrogallic acid and naphthol—drugs in common use by dermatologists—the internal use of potassium chlorate in large doses, and the ingestion of certain so-called edible fungi—marchella and helvella esculenta—are well-known causes of hæmoglobinæmia and consequent hæmoglobinuria. There are numerous other causes of these conditions to which I need not refer in detail, all of which should be excluded before the latter are regarded as effects of malarial poisoning. In addition to such negative evidence of malaria, the specific organism of the disease, the hæmatozoon malariæ, should be demonstrated. It may be said that this is asking too much of the practitioner of medicine, especially in remote country districts; and so it is, so far as concerns all practical purposes. Our confidence in quinine, however, is not to be shaken by any facts less convincing.

Dr. Vaughan: I do not believe, in the first place, that quinine has any marked tendency to cause hæmaturia. I have seen a great deal of malaria in southern Illinois, where quinine was given very freely, and hæmaturia was very infrequent. I have seen considerable malaria in Michigan, and we give quinine freely, and we do not often have hæmaturia. I never saw a case of hæmaturia which could be attributed to this drug, although I am prescribing quinine every day when at home. I have seen many untoward symptoms due to quinine—rashes, sore mouth, etc.—but I have never seen it cause hæmaturia. I once took one hundred grains of quinine at one dose, and felt marked symptoms, but had no irritation of the kidney, and certainly no hæmaturia.

The malaria of the South, where they have this hæmaturia, must be different from the malaria of the North; there must be some other factor in its production, as Dr. Atkinson has suggested. The plasmodium is the same in Illinois as it is in Louisiana, and I suppose that years ago cases of malaria in the Saginaw Valley, Michigan, were as severe as those in any part of the South, and still hæmaturia was a very rare thing in the former place.

Dr. Loving: I desire to corroborate what Dr. Vaughan has stated. During the last thirty-five years I have treated malarial fever in the city of New York, in New Grenada, the West India Islands, Indiana, and in Ohio. We

have not yet gotten rid of the malady in Ohio, and I still see cases every week. My cases (many hundreds in number) include every type of the disease—the mildest and the most malignant. In the treatment I have relied on quinine almost to the exclusion of other medicines, and have prescribed that drug in small, medium, and very large doses, but have never seen a case in which hæmaturia or hæmoglobinuria could be fairly attributed to its influence. I have seen hæmaturia and hæmatemesis in cases in which quinine was used, but the hemorrhage appeared before the administration of the medicine.

In cases such as are under discussion the causes of hemorrhage should, I think, be sought in the lesions arising from malarial infection, not in the influences of the medicine.

Dr. Hare: I have apparently led the gentlemen to misunderstand me in regard to one particular. I did not mean to urge that quinine should or should not be given. The point that I wanted to bring out is that every case is a law unto itself, and that certain cases can take quinine, and in other cases it ought not to be given.

As to the first cases which Dr. Henry reported as being cured by quinine, of course, these particular cases have no more significance than any other like number of cases, and further, quinine was not isolated at that time.

Undoubtedly, hæmoglobinuria follows hæmoglobinæmia, and I attempted to point out in my paper several causes that would produce hæmoglobinæmia. If I remember correctly, in Dr. Tyson's article in Pepper's *System of Medicine*, he stated that most of the cases that he had examined were hæmoglobinuric and not hæmaturic. I know Professor Welch, of the Johns Hopkins University, examined many cases, and found all of them were hæmoglobinuria; but, as all the specimens were sent from a distance, this would naturally be the case, from the action of the acid urine upon the corpuscles. Other equally good authorities have found the red corpuscles very frequently.

MISCONCEPTIONS AND MISNOMERS REVEALED BY MODERN GASTRIC RESEARCH.

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It is now twenty years since Murchison described the condition that we still know as lithæmia or latent gout. The late Dr. Fagge in England and Dr. Draper in this country have emphasized the importance of the disease, and the latter has given us a theory, which practice often seems to confirm, and which by many is believed to explain the relation that evidently exists between the character of the food taken and the lithæmic state.

It is needless to recall the teaching that, owing to the facility with which the carbo-hydrates appropriate the lessened amount of oxygen going to the liver, there remains too little for the proper oxidation of the nitrogenous substances, the waste of which, as a result, passes into the circulation as uric acid. It will be remembered that for this reason it is recommended that carbo-hydrates be withheld in cases of lithæmia, and that the diet be restricted to nitrogenous substances. A complete withdrawal of carbo-hydrates is advised in aggravated cases. Now the more aggravated the case, according to this contention, the more it approaches typical gout; so that but a single step is needed to bring one to the position of advising an albuminoid diet in gout. Indeed, this is the present attitude of some adherents to the belief. From this position, viz., that meats constitute the proper diet for typical gout, let us retrace our steps to the question of atypical gout and the proper diet for it.

Gout, all will acknowledge, is common in England—not merely typical gout, with occasional severe paroxysms, with arthropathies and all the train—but gout manifesting itself in a variety of ways, as, for instance, in severe and persistent headaches; but in England, instead of allowing meats to these sufferers, they are placed upon an

almost non-nitrogenous diet, and it is found that the more liberal the allowance of azotized substances the worse becomes the patient.

How is it that, with the gouty, meats disagree in England and agree in America? Observation teaches me that this difference is owing to a misconception; and that in the great majority of cases, in point of fact, an albuminoid diet is an improper diet in gout, whether it be typical or latent; but at the same time I am prepared to admit the signal benefit derived from prescribing this diet for many so-called lithæmics in this country. In plainer language, it is suggested that gout, although becoming more frequent, is still an uncommon affection in America; but, on the other hand, there is scarcely a disorder so often presenting itself to the city practitioner as that which so persistently has been called lithæmia. Wherever mental strain, "nerve-tire," and imperfect oxygenation are seen, there is witnessed that group of phenomena that is here denominated lithæmia. In all modesty let me aver that this is not gout, and that it is what Murchison described as *lithæmia* well may be doubted.

All that make careful study of such cases must be impressed with the frequency of complaint as to the primary digestion, and, if the study be thorough, this association of digestive trouble with lithæmia will be found invariable. Of course, this has not been overlooked, but the fault has been attributed to the liver. Now, habitual and painstaking examination of the stomach-contents alone is necessary to change one's belief in this matter, inconsistent as this may be with views that I held in 1885.[1] It is maintained, then, that the condition in question is a toxæmia of gastric origin, the result of wrong living, and particularly of wear and tear of the nervous system, and not the atypical expression of a mysterious, hereditary disease with its joints, its tophi, its arteries, and its kidneys.

To Leube's method of gastric aspiration we owe most of our precise knowledge of disorders of digestion, and following its use it was but natural to expect a mass of conflicting ideas as to the nature of these disturbances. Yet from this indiscriminate mass we have now some well-assured facts. We know that the normal gastric chemistry is often perverted, and that fermentable substances are capable not only of interrupting their own proper digestion, but of interfering

[1] "Nutrition in Lithæmia," Trans. N. Y. State Medical Association, 1885.

with the digestion of substances of other kinds, of throwing upon the liver the task of oxidizing materials but partly and wrongly prepared. Following this excessive demand for oxygen come imperfect disassimilation, toxæmia, uricacidæmia, and lithuria (Gouley).

What, then, is the natural indication? It would seem to be the correction of the primary digestion. Experience proves that this is not too great an assumption. Correct digestion and you correct the toxæmia. For the reason that meats are not likely to ferment, the albuminoid diet often affords at least temporary relief in these cases —relief of digestion and relief of toxæmia. This appears to be a reasonable explanation of the contradictory opinions held as to the proper diet in so-called lithæmia, and why the albuminoid diet has received so great support from the practitioners in this country as compared with that from those in England; but the albuminoid diet often fails in these cases—its adoption is followed in some by immediate aggravation of symptoms and in others not until a certain lapse of time.

This is readily explained by the systematic study of the gastric contents, for it will be seen that those that are subject to hypohydrochloric acid secretion are unable to digest meats satisfactorily, and that these substances, in fact, not infrequently undergo a putrescent decomposition in the stomach, inducing varied disturbances; the exception is when sufficient hydrochloric acid is administered after the meal to make digestion possible. When, on the other hand, there is hyper-hydrochloric acid secretion (which in the neurotic frequently occurs), the albuminoid diet often affords instant relief, because digestion becomes facilitated, the liver is no longer overtaxed and is better able to convert the proteid waste into urea, and thus the lithæmia is diminished. This will not be overcome, however, unless the patient sufficiently exercises and thereby increases oxygenation; but there will be diminished alkalinity of the blood, heightened acidity of the urine, and alkalies will be required for relief.

Undoubtedly, those that suffer from the gouty diathesis become victims of lithiasis more readily than others, but their number is relatively so small that one can say that lithæmia is an auto-infection occasioned by imperfect primary digestion, usually arising in the stomach; and the failure of this organ is the result of too feeble in-

nervation in those whose lives are relatively sedentary and whose drafts upon the nervous system are so great as to induce appetites proportionately too large for the physical activity of the organism.

The treatment, to be satisfactory, should be based upon the systematic study of gastric digestion. To resort at once to alkalies or mineral acids is to begin at the wrong end; and to advise indiscriminately an albuminoid diet, while it frequently succeeds temporarily, cannot with safety be long continued, and often fails either wholly or in part.

In point of nomenclature it is suggested that the terms lithæmia (Murchison), uricæmia (Flint), uricacidæmia (Von Jaksch), are too limited, for while the uric acid is manifestly a notorious offender, there are doubtless other more subtle and less understood substances that often find their way from the alimentary canal into the circulation, to disturb function and injure structure of various parts. To describe these states the term auto-intoxication (Bouchard) is at least suggestive. In view of the enthusiastic labors of the French in the inviting realm of gastric chemistry, we may reasonably expect a more exact knowledge of these forms of toxæmia in the future. Meantime, clinical study demonstrates their existence and importance.

From my case-books I am prepared to report a sufficient number of instances to justify the statement that neurasthenia, vertigo, persistent headache, insomnia, muscular spasm, and epileptiform convulsions; that naso-pharyngeal catarrh, laryngitis, tracheo-bronchitis, and asthma; that Bouchard's nodules, some cases of so-called arthritis deformans, and other joint troubles, not to mention a variety of minor conditions and those concerning which there is a reasonable doubt, depend upon gastro-intestinal toxæmia. At any rate, so far as space will admit, I shall append the reports of the cases referred to—cases that proved manageable by treatment directed to the digestion, as guided by a study of the gastric contents, and which in most instances had long resisted other lines of treatment. I am aware that some of these cases are open to criticism. It may be said of some that they were of reflex origin; of others, that additional factors were not excluded, and finally that the general conduct of the cases, rather than the special management, led to the improvement. In reply, it is advanced that all these objections were considered and for the most part dismissed as untenable.

In 1889 Dr. Garland read before this Association an admirable paper on "Gastric Neurasthenia," in view of which and the discussion that it provoked, I feel considerable diffidence in advancing the subject of gastric disorder as the cause of neurasthenia. Nevertheless, these cases exist, perhaps more often as the result of gastrectasis. On this subject Champagnac, in a recent monograph published in Paris, concludes:

"1. The coincidence of dilatation of the stomach and prolapse of the right kidney and neurasthenic disturbances is absolutely incontestable.

"2. One may, by directing treatment toward the dilated stomach, cure the nervous symptoms that accompany and follow dilatation.

"3. This treatment does not cause the dilatation to disappear, but prevents the auto-intoxication that is the cause of the neurasthenic symptoms.

"4. Although the gastrectasia does not disappear entirely, the patient ceases to be nervous.

"5. In the pathogenesis of neurasthenic disturbances we do not admit the theory of Glenard—enteroptosis—but that of Bouchard—the pathogenic importance of dilatation of the stomach."

While not maintaining that the stomach is always responsible for neurasthenia, yet with most of these observations I am in perfect accord, convinced by many such cases as those herewith reported, and including all except those numbered I., II., IV., V., XI., and XII. Neurologists have long been alive to the importance of attending to the primary digestion in epilepsy. I report two of several cases of epileptiform convulsions that I have seen relieved by treatment of the stomach, and in none of these were dyspeptic symptoms complained of. The first case is of unusual interest:

G. N., twelve years old, was the only daughter of healthy parents. A cousin of her father was epileptic; a cousin of her mother was insane. The family history was otherwise good. The patient had an enormous appetite, and no symptoms of indigestion save a coated tongue. She had never menstruated. The urine was normal. In September, 1890, during the night, she had her first seizure. There was tonic followed by clonic spasm, which was succeeded by a period of coma. There was no recollection of the attack. The seizures were repeated twice before January, 1891. Examination showed no physical defect save gastrectasis and slight hypermetropia (O. D. = 20/XVIII. O. S. = 20/XVIII). The equilibrium of the ocular muscles was normal. The ophthalmoscope indicated practically emmetropia. The voracious appetite led to an investigation of the digestive tract. On February 23, 1891, after a test meal, I withdrew the stomach-contents. There were found present berries

taken the day before, bread taken eight hours before, an abundance of ropy mucus, and free hydrochloric acid. A restricted diet and lavage secured immediate relief. Treatment was continued until May. From this time the patient seemed perfectly well; the stomach was much smaller; the appetite natural, and there were no convulsions. One year later the patient was reported well, with no return of her trouble.

The second case occurred in a young woman (Case I.). I have seen men similarly affected and relieved.

As to naso-pharyngeal and tracheo-bronchial catarrh, associated with and frequently dependent upon gastric disturbances, the cases are so numerous that they no longer excite special interest. One case only is reported, although the list might be made long:

Mr. L., a merchant, forty-five years old, had suffered from catarrh of the upper air-passages for years; he vomited a quantity of mucus each morning; he also had acne rosacea. Local treatment afforded relief, but not cure. Examination of the stomach-contents revealed an excess of free hydrochloric acid, with pronounced gastric catarrh. Appropriate diet and treatment relieved all of the symptoms. There was sufficient emphysema to keep up gastric congestion. Indiscretion in diet reëstablished the gastric disturbance, with a renewal of the trouble in the upper air-passages.

The well-known relation existing between asthma (Case IV.) and the state of digestion forbids more than mention of the matter here, but the dyspnœa attending certain cardiac disturbances in which there may be also incompetency of the kidneys is, to a great extent, dependent upon gastro-intestinal infection, as demonstrated by Huchard and his assistant, Tournier (*Bulletin Medical*. No. 19, 1892).

As to the causation of headache, it would seem that we should ascribe a larger proportion of cases to the stomach. One is too likely to turn away from this inquiry after having heard that there are no gastric symptoms, when in fact some of the most intractable cases of indigestion conceal themselves behind symptoms referred to remote parts. This is well shown by Westphalen,[1] and also by my own cases reported (Cases II., III., V., VIII., and XV.). Similar statements apply to habitual insomnia (see Cases V., VI., VII., XV., and XVI.), and also to grave and mild forms of anæmia (see

[1] Berliner klin. Wochenschrift, 1891, No. 37.

Cases X. and XII.), a matter that has the support of Pick,[1] of Nothnagel's clinic.

Of late, few subjects in medicine have attracted greater interest than the nature of certain arthropathies. The matter is introduced here because there is reason to believe that, since the joint-troubles of rheumatism, gout, gonorrhœa, and scarlatina, not to mention more, depend upon special forms of toxæmia, so may still other joint-troubles depend upon toxæmia not yet so clearly specialized. Dr. Edward Blake, of London (*Am. Journal of the Med. Sciences*, 1892, No. 2), reports instances of rheumatoid arthritis depending among other things upon oral sepsis occasioned by a faulty plate of artificial teeth. I have seen a case relieved completely by removal of old fangs and correction of a disturbing plate. Years ago, Bouchard directed attention to certain nodules appearing upon the phalangeal joints of the hands in victims of dilated stomach. The importance given this matter in Paris may be estimated by the discussion reported in *Le Bulletin Médical*, 1892, No. 23. Certainly these joint-troubles are extremely common in chronic dyspeptics, and while they are sometimes found when no symptoms of indigestion are discovered, there is reason for the belief that in these cases the joint-affections depend upon gastric trouble that is past or unrevealed. Pseudo-rheumatisms of infectious origin are seen to be common when searched for, and not rarely, in my opinion, they are gastro-intestinal in source.

The following case is interesting in this connection:

Mrs. H., thirty-three years old, had always suffered from languor, loss of flesh, and diminished power of endurance. Two years ago she suffered from what was called an appendicitis. From this she was restored to her usual health. Her blood was found lacking 50 per cent. in hæmoglobin. She complained that for years she had experienced fugitive pains in her joints, particularly in the knees, and for several months forced flexion of these joints had been attended with a sensation of crepitation, which not only could be felt, but heard at considerable distance. These joints were somewhat enlarged. Recently the joints of the upper extremities had become stiff, swollen, and moderately painful, especially when moved. The woman's appetite was excellent, and she stated that she had never had the slightest trouble with digestion, although her bowels were not active. The urine showed an abundance of calcium oxalate crystals, but was otherwise negative. Searching for the cause of her anæmia, the stomach was found to be too large, and there was

[1] Wiener klin. Wochenschrift, 1891, No. 50.

marked *clapotage*. Although vague, there was sufficient evidence of gastro-intestinal disturbance to justify investigation. Accordingly lavage was practised three hours after a test-meal, and the stomach found to contain no food; but there was present lactic acid in considerable quantity. The intervals between the meals and the aspirations of the stomach were now progressively shortened, but the result was the same until at last, thirty minutes after eating a hearty luncheon, all the food was found present, with an abundance of lactic, but with no hydrochloric acid.

It was now determined to administer hydrochloric acid; 1.50 grammes of dilute acid, in divided doses, were given after each meal; and gastric faradization was employed. Immediately thereafter food was found present; the digestion was slow, but still no hydrochloric acid was discovered. The patient, however, was promptly relieved in every way; the pains ceased, the stiffness of joints disappeared, and there was the most surprising improvement in her appearance. She gained four pounds in weight, the color returned, the bowels became regular, and she declared that she had not felt so well in five years. This state continued for some weeks, but then elapsed a week without treatment, during which the patient had an experience that fatigued her mentally, and she reported that her symptoms had all returned; there were languor and depression of spirits; the joints were again painful and stiff. Naturally, I prophesied that her stomach would be found empty again, and upon examination this proved to be the case; moreover, the lactic acid that had disappeared was again present in quantity.

This case is still progressing and under treatment, but its history is certainly instructive in the highest degree.

A tabular statement of the examinations is introduced here for convenient study:

Date.	Period after meal.	State of stomach and its contents.	Lactic acid.	Hydrochloric acid.
Feb. 29	3 hours	Empty	Present	Absent.
March 2	4 "	Empty	"	"
March 4	2.30 "	Empty	"	"
March 8	2 "	Empty	"	"
March 12	30 minutes	All food present undigested; general meal.	"	"
March 14	1 hour	Practically empty. Prescribed hydrochloric acid and gastric faradization.	"	"
March 16	1.15 hours	Food present	"	"
March 19	1.15 "	Food present	"	"
March 21	1.15 "	Food all present. Feels much better. Joint-pains gone	"	"
March 25	4 "	Food all present. Is better . . .	"	"
March 28	3.30 "	Much food present. Has not felt so well in years.	Absent	"
April 5	2.30 "	Food present	"	"
April 7	2 "	Food present	"	"
April 25	3.45 "	Empty. Pain and swelling returned. Feels badly.	Present	"

What impresses me most is the frequency with which patients present themselves for relief of anæmia, asthma, headache, insomnia, diarrhœa, constipation, muddy skins, and irritable kidneys, who make little or no complaint of the stomach, and yet whose troubles arise primarily from the stomach, and who by treatment directed to that organ only can be relieved.

The relations existing between disturbances of the digestive tract and the chronic diseases of those great eliminative organs, the lungs, the liver, and the kidneys, have not received that attention which the future will declare to be imperative. Literature now bristles with contributions thus directed, and in appreciating that the microörganisms that invade our bodies are pathogenic in proportion to the toxines that they develop, we are coming to perceive that very many morbid states hitherto misconceived, and sometimes misnamed, are merely results of auto-intoxication; that the excretory organs that so generally fail and decay would not thus suffer but for the unnecessary strain imposed upon them through the mischief arising in the gastro-intestinal tract.

Report of Cases.

Case I.—Miss B., aged twenty-five years, had for many years been weak and listless, and had convulsive seizures of an epileptiform character. She had slight astigmatism, which was corrected without benefit to the general health. She complained chiefly of attacks of unconsciousness. Examination disclosed gastrectasia, with excess of hydrochloric acid, catarrh, and variable digestion. Treatment by lavage and the direct application of the interrupted current, with suitable diet and gastric medication, resulted in the disappearance of the convulsions and the restoration of the general health.

Case II.—Miss R., aged twenty-one years, had severe, frequent, and persistent headache that nothing relieved. Examination of the stomach revealed decided gastrectasia, with hyper-hydrochloric acid secretion. Treatment by lavage and the direct interrupted current for several months, together with proper diet and but little medication, resulted in a cure.

Case III.—Mrs. G., aged twenty-eight years, had aggravated headaches, vertical and occipital, for many months. Meeting people, conversation, or reading gave her great distress. She was intensely nervous and weak. The eyes had been properly examined and corrected. The pelvic organs were sound. She had tried many things in a search for relief, but without success. Disturbance of vision accompanied the headaches. She complained of slight dyspepsia. Examination disclosed the existence of a dilated stomach—the lower border reaching about four inches below the umbilicus—catarrh, hypohydrochloric acid secretion, slow digestion, fermentation, and constipation.

Treatment by lavage and the direct interrupted current for some months brought about relief from the headaches and disturbed vision, with quite marked improvement in the general health. The lower border of the stomach rose to the level of the umbilicus, and the patient considers herself well.

Case IV.—Miss N., aged thirty-three years, complained of flatulency, gastric distress, eructations, and attacks of dyspnœa that she called asthma. These last were accompanied by regurgitation of mucus from the œsophagus, and a mucous discharge from the trachea, lasting two or three hours only. The paroxysms were sometimes intense and accompanied with great circulatory disturbance. The pulse in the intervals was slow and hard, the left ventricle undergoing hypertrophy. There were also areas of superficial anæsthesia. Examination of the stomach revealed gastric hypotony, hypo-hydrochloric acid secretion, and catarrh. Treatment by lavage, restricted diet, predigested foods, and asafœtida resulted in cure. She has recently had a recurrence.

Case V.—Captain B., aged forty-eight years, formerly a shipmaster, now an agent, from leading a sedentary life has suffered from insomnia, with headache and nervous irritability. He has had belching of gas and sour stomach. Examination revealed a somewhat dilated stomach, with slow digestion and fermentation. He was treated by means of lavage and gastric antiseptics. His insomnia was immediately relieved. He improved steadily and completed his recovery by a transatlantic voyage.

Case VI.—Mr. W., aged fifty-five years, had gastrectasia with hyperhydrochloric acid secretion and *phosphaturia*. He was reduced in flesh and strength, had cardiac palpitation, mental restlessness, persistent insomnia, gastric uneasiness, and melancholia with delusions. Treatment by lavage and the faradic current applied directly resulted in marked amelioration of the symptoms and great improvement in sleep. The man was under treatment for three months, after which he was able to return to business; and although not well, his mind was sound, and he was every way much better.

Case VII.—Mrs. W. A., aged thirty-six years, suffered from pain in the left hypochondrium, disturbed sleep, inability to sustain mental or physical effort, and debility. She has a wandering left kidney. She had gastric distress, with fermentation and eructations of gas, but no vomiting. The urine at first showed excess of acid, later an excess of phosphates. Examination of the stomach showed great irregularity in digestive strength and secretions, with extensive catarrh. Digestion was usually slow. There was hypotony. She was treated by means of lavage and the faradic current, sometimes the continuous current. Improvement in the general condition was in ratio to the improvement in the gastric state. She was discharged after four months, improved, but not cured.

Case VIII.—Miss H. R., aged twenty-one years, has suffered for two years from general debility, occipital headache, depression of spirits, and inability to work. Upon two occasions she has spat blood. The case had been considered tuberculous. No bacilli were found in the sputum. She had few symptoms of gastric disturbance. Examination revealed extensive dilatation, with irregularity of the secretions. Treatment by lavage and gastric fara-

dization was continued for six months, resulting, after a sojourn of two months in the mountains, in a complete cure. She gained fourteen pounds in weight, and particularly showed improvement in the nervous system and in her power of endurance.

Case IX.—Miss D., aged eighteen years, a farmer's daughter, has suffered for three years from general neurasthenia with headache, fainting spells, and inability to exercise even slightly. She spent most of her time in bed and was despondent, fretful, and peevish. The urine contained an excess of lithic acid and lithates. The bowels were constipated; the skin discolored. The girl regurgitated food, belched gas, and had pyrosis and nausea. Examination showed the stomach to be slightly dilated, and usually with an excess of hydrochloric acid. Lavage was employed for several months, and occasionally the continuous current. She was placed upon an albuminoid diet and occasionally given predigested milk; later, the diet was made more general and tonics were administered. Her improvement began with the advance in her digestive power. After four months she was discharged much improved, and has continued gaining during the past year.

Case X.—Miss B. C., aged twenty-eight years, suffered from depression of spirits, mental and physical prostration, and profound anæmia (the blood contained only 40 per cent. of hæmoglobin). She suffered from gastric distress. Examination showed the lower border of the stomach to be four inches below the umbilicus; there were fermentation and extensive gastric catarrh. She was treated by Dr. Allen A. Jones for five months by means of lavage and the faradic current at night. Her stomach returned to its normal size, and digestion became satisfactory. The patient was discharged, recovered, with a disappearance of the nervous symptoms.

Case XI.—Mrs. D., aged forty years, complained of occipital headaches, with attacks of vomiting, that would last for several days, and were accompanied with great prostration. There was gastrectasis; the lower border of the stomach extended four inches below the umbilicus. There were some catarrh and hypotony (hydrochloric acid was deficient). The woman was treated by means of lavage and internal faradization for three months. There was great improvement in every way, which has continued since the cessation of treatment.

Case XII.—Mrs. C. B. G., aged twenty-six years, suffers from weakness, anæmia, bronzed skin, with occasional chills, followed by elevation of temperature, lasting for several days. She has moderate gastric dilatation and poor and slow digestion, with hypotony. There is an absence of hydrochloric acid and sometimes an excess of lactic and fatty acids. Treatment by lavage, faradization, hydrochloric acid and other digestants, and nux vomica and physostigma was instituted. Great improvement followed. After two months the patient was sent to Florida and returned well.

Case XIII.—Mrs. G. S., aged twenty-six years, manifested a condition of neurasthenia, with gastric pain, nausea, and gas. Examination revealed a great excess of hydrochloric acid, with slow digestion of carbohydrates.

Treatment by diet and antacids, as governed by the examination of the stomach-contents, was adopted. The patient was discharged after six months and is now well, although not particularly strong.

Case XIV.—Miss E. W., aged twenty-two years, who has a neurotic family history, complains of great fatigue, made worse by mental exertion. She also has headache, and complains of burning in the epigastrium. She was found to have most marked dilatation, with very slow digestion and great excess of hydrochloric acid and some catarrh. She has been under treatment for six months, and has improved, but is not well. She is benefited by strontium bromide and other gastric sedatives. The diet can be regulated only after examination of stomach-contents. The condition is improved by lavage.

Case XV.—Mrs. S. S., aged twenty-five years, belongs to a family of neurotics, one sister being a complete wreck from neurasthenia. The patient suffers from weakness, insomnia, headache, inability to sustain efforts of any kind, and backache. She is disturbed by light and by sound. She has a stomach of irregular size, sometimes found two or three inches below the umbilicus, while sometimes it is of proper size. The gastric secretions are also irregular. Digestion is sometimes rapid, sometimes slow. After treatment by lavage, electricity, and rest, the improvement in the state of the stomach was rapid and evident, and this was followed by improvement in the general condition. She is now progressing favorably.

Case XVI.—Miss S., aged forty-two years, has suffered from dyspepsia since she was twenty. She has had two attacks of "exhaustion." She has also had typhoid fever. For the past ten years she has suffered from neurasthenia, showing itself in insomnia, occipital headache, weakness of vision, cold hands and feet, inability to sustain mental or physical efforts, and constipation. Examination shows the stomach to be moderately dilated, digestion to be slow, and accompanied with fermentation and gas. Hydrochloric acid is absent. After treatment by lavage, electricity, diet, and purgatives for three months, the woman was discharged well.

DISCUSSION.

Dr. Musser: I quite agree as to the necessity for local treatment in such cases, but I want to emphasize the necessity of general treatment and management of such cases. In my conduct of such cases I have always been impressed with the efficacy and necessity of general treatment and management, the gastric condition being secondary. It seems to me that all such cases, in general, may be said to be cases that arise from excessive wear and tear, and there is a lessened amount of capital from which to supply the material necessary to keep up the processes of life, and in order to secure more capital, whether by local treatment or general management, you must add to their

nutrition. I prefer to look at these cases in a general way and to treat them in the light of such general views as to their nature and origin.

Dr. Lyman: I wish to say a word in the direction indicated by Dr. Musser, on the importance of considering the general condition of the patient. The etiology of these cases is generally connected with scrofula, or the arthritic diathesis. The arthritic diathesis predisposes most remarkably to all these local disorders that the doctor has emphasized, and it is important to recognize the connection of the local disease with that general substratum. The topical treatment, however, is not rendered any the less necessary. We see this illustrated in a certain class of gynecological cases in which the topical treatment is just as important as the general, and without general treatment the topical treatment is a tedious affair. So in the gastric cases, there is a diathesis underlying the whole difficulty, and we must direct our treatment to this diathesis at the same time that we use these local applications.

Dr. Stockton: I do not wish to be understood as advocating the treatment of these affections by any special plan of gastric medication, or lavage, nor do I wish to be understood as forgetting the importance of the general management of these cases. I do wish to insist upon the absolute importance of guiding the general management of these cases upon the findings from examination of the stomach. It does not mean that the patient should receive special treatment by electricity, or lavage, or hydrochloric acid, or alkalies, but it means acting intelligently. Just as our knowledge of certain diseases is improved by examination of the eye and the urine, so I think our knowledge will be improved by examining the contents of the stomach. I think it is a mistake to regard these cases from the general standpoint as much as we have been in the habit of doing. While we should recognize that there is a failure in the nervous system, we should also realize that when the stomach fails we have toxæmias which give rise to a great variety of evils, and by preventing these toxæmias we relieve our patient.

THE PRODUCTION OF TUBULAR BREATHING IN CONSOLIDATION AND OTHER CONDITIONS OF THE LUNGS.

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The title of this paper is perhaps subject to misconception. It includes the discussion of the physical principles involved in the production of tubular breathing, and suggests that these same principles induce broncho-vesicular and cavernous breathing, which differ from the former only in degree. There has been some little controversy upon this subject, limited, however, largely to those authors who have practical minds and a fancy for acoustics.

Most of our modern text-books contain descriptions of the sound, and account for its production by quoting one of the few authorities who have written on the subject. The explanation offered by Laennec, and still held by some, was that the sound was produced by the vesicular murmur being cut off and the tubular or bronchial sound alone being audible. He expresses himself as follows in the fourth edition of his work:

"The sound observed in the larynx, trachea, and larger bronchial trunks is due to the absence of that slight crepitation which accompanies the dilatation of the air-cells of the lungs, and the idea of a drier sound is suggested to us. It is strong in most parts of the neck. When the texture of the lungs becomes indurated or condensed from any cause, such as pleuritic effusion or the changes occasioned by a severe peri-pneumony or hymophysis, the vesicular respiration having then disappeared, or being much lessened, we can frequently perceive distinctly the bronchial respiration, not only in the large, but even in the small ramifications of the bronchi. The cause of this bronchial respiration appears to me very obvious, in fact, when the air is prevented from penetrating the cells this is the only kind of respiration that can exist, and is louder and more distinct in proportion as the lung is more condensed and thereby becomes a better conductor of sound."

Dance, a French authority of later date, adopts virtually the views of Laennec, and states in the *Dictionnaire de Médecine ou Repertoire Général des Sciences Médicales* of 1833, that bronchial breathing is present when the air passes through the bronchial tubes without reaching the pulmonary cells. It produces in the ear a sensation of columns of air winding in the tubes of a certain caliber without the sound of vesicular expansion; that sometimes the sound is so intense that it would seem the patient's breath was passing through the stethoscope instead of through the bronchial passages.

Skoda thought that the tubular breathing was the transmitted laryngeal sound intensified or otherwise altered through what he called consonance, but he does not use the word in its ordinary acoustic sense, but explains that he applies it with the compound meaning of consonance and resonance, applying the principles of the sounding-board to obtain the intensity which he suggests. He does not make his views very clear, except so far as the principle is concerned. The following is a translation of what is written in his *Abhandlung über Perkussion und Auskultation:*

Bronchial breathing can be higher, stronger, deeper, or weaker, or even just as high and strong as laryngeal breathing, and is due to consonance in sound in the upper and lower portions of the air-passages, and the difference in volume and pitch depends on the condition of the inner lining of the air-passages in admitting of the production of the consonant sounds.

The most elaborate treatment of this subject that has come to my notice is found in Flint on the *Respiratory Organs.* Here Austin Flint devotes considerable space on this subject, and concludes by regarding

"bronchial respiration as consisting of transmitted sounds; they are produced within the trachea and primary bronchi, and probably also within the subdivisions of the latter, and are conducted by the air in the tubes and the consolidated lung to the ear of the auscultator. In what proportion they are due to the trachea and the larger bronchi exterior to the lungs, and to what extent sounds generated within the pulmonary bronchial subdivisions may be combined, are points not easily determined."

Flint certainly had an analytical mind, and his description is the most satisfactory. More modern writers adopt this view without

notable modification. Guttmann devotes fair consideration to the opinions of others, but expresses his views as follows:

"Bronchial respiratory murmur heard in disease is nothing more than the laryngeal sound carried with scarcely diminished intensity through consolidated lung-tissue."

The views of R. C. M. Page and Vierordt are virtually the same. So also are those of S. S. Burt, excepting that the latter speaks of the sound being transmitted through the bronchial tubes as through a speaking-tube, directly to the surface and ear of the auscultator. As will be observed, there is no great variety of opinion, and without quoting at greater length to prove the statement, which would but occupy all my allotted time, they are not fully satisfied with their own explanation, for they quite universally acknowledge differences of pitch over different regions in the same individual, and even contrast the laryngeal and tubular pitch, pointing out differences, which all will concede could not be, if the source of the sound were the same, for pitch cannot be altered by the medium of transmission, and, as Dr. Flint says,

"there are circumstances which give rise to variations in pitch which we do not understand, and that the sounds generated within the trachea and bronchi, as in conditions of health, will not suffice to explain the intensification of sound which sometimes characterizes bronchial respiration in disease, nor the disparity in pitch which is observed." He further concludes that "other physical influences are doubtless involved which are not as yet satisfactorily explained."

Dr. J. Bloodgood, of Chicago, published an article on this subject in 1860 which has not received the consideration which it deserves, and my attention was only called to it within the past few days. In this article it is claimed that hepatization is not necessary for the production of tubular breathing, and that the normal lung-tissue does offer a good medium for conducting sound, as demonstrated by the clearness with which sibilant râles are heard when the parenchyma is normal; that when a bronchus becomes temporarily blocked by viscid mucus a clear, tubular sound is at once detected which disappears when the secretion is coughed up; that during the time it is heard the lungs are normal. Dr. Bloodgood argues from this that the air in its passage downward is diverted into many tubes, the aggregate capacity of which is much greater than the trachea

and bronchi; that it therefore rushes slower and slower the deeper it penetrates; that should a small bronchus become plugged at a little distance from its origin, or lead to cells filled with inflammatory product, it would furnish a cavity analogous to the Pandean pipe, and yield a tone determined by its size; that if it were located high up in the lungs, where the air has the greatest velocity, it would be intense, but if located in the lower lobes the sound would not be induced, or, if present, the intensity would be diminished. His argument is based upon false anatomical grounds, and he does not accord the transmitted laryngo-tracheal sound its place.

I began, about three years ago, a line of work and experimentation having the great charm called original work, which always acts as a wholesome spur, and after eighteen months of time it developed most successful results; but in that time I also made the discovery that my undertaking was not new, though I had succeeded without the knowledge that the ground had already been staked out by others. The work referred to is the making of casts of the air-passages, and for that purpose I used an alloy composed of tin, 4 parts; lead, 8; bismuth, 15; and cadmium, 3. This alloy softens at 60° centigrade, and fuses at 65°.

I exhibit the castings which I made at that time with some little reluctance, as I do not know how they may compare with those whose opportunities may have been better than mine, and who may have pursued their work longer than I did, for I have never seen any other castings of this kind; but my object in showing them is only to illustrate the basis of the explanation here advanced as to the causes that contribute in the production of that peculiar sound which we all term tubular or bronchial breathing. These castings, which I invite you to examine, are made from healthy lungs, which should be procured as soon after death as possible, and the cast is formed by pouring the alloy of low fusion into the trachea and allowing it to penetrate as far as possible into the tubes and vesicles before it chills and consolidates. It hardens almost immediately into this solder-like form, and the lung is then macerated in caustic soda, and eaten off, which leaves the casting, as you see it, representing what must be the exact caliber and shape of the air-passages, as far as the metal has penetrated without burning or destroying the pulmonary tissue. I need not remind you that success does not attend each

attempt, that the degree of heat, the pressure and the presence of moisture, will modify the result and act as factors in the frequent failures, and determine the degree of success. In most of these castings were obtained of the larger bronchial tubes, in some, the most minute tubular subdivisions, and in a few the surrounding vesicles.

Wherever the vesicular castings were obtained the tubes were, of course, hidden from view. They were also not complete throughout the lung, and were often unavoidably broken off, even by their own weight, in the preparation. Human lungs do not prove good specimens unless procured from subjects dying from hemorrhage and after short illness, as the mucus, which is always present, debars the possibility of a perfect cast. The preparations here exhibited were made from adult and infant human lungs, and the lungs of sheep, calves, dogs, and rabbits. In many cases the alloy was poured into the trachea while the lungs were still *in situ*.

It is not within the province of this paper to discuss the anatomy of the lungs or to point out the errors which exist in some of our best descriptive anatomies; but I particularly invite your attention to the method of division or branching of the bronchial tubes, which quite uniformly takes place at about the same angle, and uniformly by bifurcation, and that the air only reaches the air-cells after passing through a long route and varying its course at the different points of bifurcation. Furthermore, at these points there is a sharp edge to the bronchial tube which acts as a prow to cut the column of air at the bifurcation. This cutting-edge is described in Sappey's *Descriptive Anatomy*, and he says that on a level of each division one sees in the cavity of the bronchial tubes a spur or prow to cut the column of inspired air. In the bronchi given off at an acute angle this spur is very pronounced and very sharp. In collapsed lungs the bronchi are naturally much diminished in size, and this cutting-edge is not very apparent, as it is not thrown out in relief, but in consolidated lungs, as in pneumonia, it is readily seen.

I am confident that bronchial breathing is a mixed sound, composed of laryngo-tracheal and cavernous elements, the laryngo-tracheal sound being transmitted through the bronchial tubes by the air in their cavities, thence communicated to the consolidated or compressed lung to the chest-wall, and heard by the auscultator, diminished in intensity according to the lack of transmitting power

of the different media through which it has to pass; that added to this sound in proportions differing under different circumstances, but often predominating in volume, is a *tubular blow* which is produced by the air rushing over the open and cavernous mouth of a patulous bronchus which leads to a lung not receiving its quantum of in-rushing air.

Now bearing in mind the cavities represented by these bronchial tubes either of the first, second, or third magnitude, the air-cutting edge referred to by Sappey, at the point of bifurcation, and I believe we have the explanation needed for variations in pitch as well as one of the contributing elements in inducing tubular breathing, and furthermore the same tubular blow will be induced whether the air is passing in or out of the lungs.

To illustrate this point more fully I have five figures, of purely a conventional character, to illustrate how tubular breathing can be produced in (1) the higher grades of pneumonia with consolidation; (2) pleurisy with effusion where the lung is in contact with the chest-wall; (3) in necrosis with a cavity, and (4) how it could not be heard in cases of effusion where fluid intervened between the lung and the chest-wall. In all of these cases it is apparent that over areas where the tubular breathing is heard there is diminished or suppressed vesicular expansion. Under these circumstances it can hardly be questioned but that the air to reach other portions of the lung rushes by and over the bronchus leading to the diseased portion, to fill the air-vesicles which do expand, and that at the point of departure the cutting-edge described by Sappey must produce a reverberation imparting a sound analogous to what would be produced by blowing over a test-tube; and it has a pitch depending on the length and caliber of this bronchus, which is the additional sound, which, for lack of a better term, I have called the *bronchial blow*. If the rush of air to other parts of the lungs is rapid, the intensity of this sound will be augmented. If the size of the tube be small and shallow, its pitch will be raised; if large and deep, the pitch relatively lowered; but in any case higher than a laryngo-tracheal sound, except in conditions of disease of the larynx, in which case its pitch might be raised much above the normal.

When this sound is intense, as we find it in the rapid breathing of acute pneumonia or extensive effusion, with lung pressed or bound to

the thoracic wall, it contributes largely toward the sounds heard, thus raising the pitch and augmenting the intensity. Should rapid breathing subside in the cases above named, or should secretion obstruct the mouth of the tube, or fill its cavity, then the intensity of this element would diminish or the sound entirely disappear. The pitch of this blowing sound is determined, as has just been stated, by acoustic laws, and depends upon the length of the bronchus and its caliber at its point of departure.

The principle is susceptible of ready demonstration with apparatus to be found in any of our offices; blowing over a small test-tube will yield a certain pitch, and filling it partially with water the pitch will be raised; a small, long tube will give a low-pitched sound; a flask may be treated in the same way to illustrate the reverberation in a cavity. This experiment may serve to explain how, after a short lapse of time, both pitch and intensity of sound may be altered in conditions of consolidation by the presence of secretion in the tubes.

I would further offer as an explanation for the exaggeration of the tubular element heard over the cavities, particularly when they are near the surface, that the intensity is very much augmented by the proximity of the sound to the ear of the auscultator, and this rule applies equally to all physical sounds, and the further we go from the point of its production the less audible it becomes. It is for this reason that sounds sometimes are limited to very small areas, particularly where the medium of transmission is poor; again, sounds cannot be heard with distinctness which are produced externally to the larynx, and those which are most distinctly heard are produced at the periphery of the air-passages or near the ear of the auscultator; labial sounds, such as chirping and whistling, are only heard as transmitted by the external air; they are never intense, whereas any artificial means which produces a rush of air in the respiratory track nearer the ear is markedly exaggerated, as, for instance, the expiratory "puffs" which are produced in this way; whisperings are intensified in like manner, and the intensity of sound at different periods of respiration depends upon the same law.

I do not think it would be possible to state what proportion of the sound is attributable to the different elements comprising it, for I am convinced that the proportion varies notably with different degrees of consolidation and under varying conditions, which would be for-

eign to my purpose to discuss here. It seems to me that the reason why this explanation has not been offered before is because the size of the tubes has been very much underrated by those who are in the habit of making physical examinations; commonly when examined the lungs are collapsed and the bronchi are diminished in size, but by noting these castings it will be seen that there are fully sixty tubes in the human lungs capable of inducing a bronchial blowing sound, while several bronchial casts in distended lungs have a diameter of about half an inch in the clear; these latter would certainly yield a volume of sound.

Before closing, I would not be understood as saying that the larynx does not play a *rôle*, and a very important one, in determining the pitch and quality of bronchial breathing, for I have experimented upon some of the lower animals, inducing a pulmonary consolidation, and with an opening into the trachea I have been able to cut off the laryngeal sound at will; from this experiment, although it was not complete, for I found it difficult to produce a pneumonia at will in a dog, I was convinced that the larynx as well as trachea and *bronchial blow* were the three elements, which, in the aggregate, induce the sound which has been the subject of this paper.

DISCUSSION.

Dr. Tyson: Dr. Cary's paper has been of intense interest to me, and the privilege of seeing his preparations is certainly one which cannot be too highly appreciated.

If I gather correctly the doctor's idea in regard to the cause of the tubal breathing, it is that this ridge or elevation at the bifurcation of the trachea, and corresponding to the rim of a test-tube, is the cause which throws the column of air into vibration and produces the bronchial breathing, and that even the tubular sound which we hear in health by placing the stethoscope over the trachea, is similarly produced as a blowing sound is produced by blowing across the rim of a test-tube. The edges of the rima glottidis probably act similarly, throwing the column of air in the trachea into vibration and producing the tracheal sound which is continued on into the branches of the trachea, fortified by the further sound caused by the ridge at the bifurcation.

Dr. Mason: These beautiful specimens, and the comprehensive and clear way in which Dr. Cary has illustrated the matter, leave little to be said.

I have often been in doubt, in examining cases with pleural effusion, as to why in some cases we get bronchial breathing and in others, with apparently a similar amount of fluid, we do not. I suppose, from Dr. Cary's remarks and the fourth diagram, that his explanation would be that fluid or air must surround the lung in order to cut off the breath-sounds altogether, and it has seemed to me sometimes that the presence of pleural adhesions might account for tubular breathing in the cases referred to.

Dr. Hare: I am indebted to Dr. Cary for giving me some new points, which I shall be glad in turn to give to my pupils. We must remember, in connection with the illustration with the test-tube, that the openings of the bronchial tubes are not absolutely rigid, but are to a great extent elastic, and the more elastic and yielding the tube the less the sound. In breathing, the air in inspiration and expiration must flow with comparatively little force, and blowing over an opening would make a noise hardly to be compared with that produced by the forcible expulsion of air which we obtain in blowing over a test-tube or a key.

I do not want to throw any doubt upon the results which Dr. Cary has reached, but simply to guard against accepting the view that the sound is almost entirely due to the passage of air over these openings. I understood Dr. Cary to state that the laryngeal and tracheal sounds were transmitted down to these bronchial tubes in addition to those sounds made by the air passing over the bronchial openings.

Dr. Griffith: I must confess, also, that I have entertained the belief that the laryngeal element is the prime factor in producing the sounds which we hear in the lung. I do not know whether Dr. Cary meant that the bronchial blow was only an added factor which gave to a large extent the element of pitch. I have often found that the most confusing auscultatory sounds were those which seem to be produced highest up. There is nothing louder and more distinct than the sibilant and sonorous râles which we know are produced high up. Sometimes these sounds are more audible from the mouth than at the chest, although also heard quite loud at the chest. I have often noticed that a child who is breathing with a distinct rattle in the larynx will seem, on superficial examination, to have the chest crowded with coarse râles. Since all these sounds are so loud I cannot but feel that this indicates that the predominating factor in auscultatory sounds is the element produced higher in the passage.

What Dr. Mason has alluded to has often been puzzling to me, namely, the frequency with which bronchial breathing is heard in large pleural effusions. I once believed that I could diagnose with absolute certainty between pneumonia and pleural effusion, but the older I grow the more I am coming to the conclusion that I can do nothing of the sort. I wish no one else to make mistakes in diagnosis, but I will admit that it is at least comforting to find the masters in the profession also making mistakes in this matter.

I would like to ask Dr. Cary, if, from his study of the anatomy of the

lung, he has come to any positive conclusion as to why prolonged respiration is greater at the right apex than at the left. I have, of course, read explanations of this difference, but none that were entirely satisfactory.

Dr. Lyman: Dr. Cary's preparations form the most interesting anatomical exhibition of the kind I have ever witnessed. With regard to the pitch of the auscultatory sounds, a thought has occurred to me which I throw out for Dr. Cary's consideration. Amongst the many other factors that go to make up these complex sounds may there not be one which is not generally appreciated? When waves of sound are multiplied upon the ear at an increasing rate the pitch of the sound is raised, while if the number of waves are diminished the pitch of the sound is lowered. This is illustrated in the locomotive-whistle, which rises in pitch as the locomotive approaches and falls as it recedes. Now, when the air-current from the trachea and larger bronchial tubes comes into the smaller bronchial tubes there must be a diminution in the rate of movement of the current, and the pitch of the sounds that are originated by its entrance into each successive bronchiole would, therefore, be lowered as it reaches the terminal bronchioles and lower and outer parts of the lung. In opposition to this is the fact that the waves thus produced are approaching the ear of the auscultator, and consequently there is a multiplication of waves upon the tympanum, derived from the successive sources of sound as the tide of air enters each bronchiole, like waves from an approaching locomotive-whistle, which would raise the pitch of the sound. The difference of pitch that is heard in the trachea and the pitch that is heard at the outer portion of the lung is the difference between these two factors. This is only a thought that has hastily passed through my mind, and it is probably after all of a purely theoretical value, since no ear could distinguish such slight differences.

Dr. Cary: As to the point raised by Dr. Lyman in regard to distance diminishing pitch: The distance would undoubtedly diminish the intensity or volume of sound, but it would not alter the pitch in any way.

The question has been raised as to the cause of the greater intensity of tubular breathing over the right apex as compared with the left. The explanation is that the tube that goes to the upper part of the right lung starts nearer the thoracic wall, and begins much higher up than any of those that go to the left lung. This is shown in the castings.

As to the point raised by Dr. Hare: I do not mean to imply that there is anything like a whistling sound produced. It is not that class of sound that I refer to; it is the reverberation in the cavity of the tube without producing a note. So far as the comparison with a glass tube is concerned, I did not intend to imply that the bronchial tubes would have the same resisting power as glass, but they do have cartilaginous rings that will maintain them as a cavity. The larger bronchial cartilages will maintain their shape in spite of the most continuous pressure from fluid outside or from inflammatory exudate.

The tubes will, of course, be diminished in calibre, but only so far as it can be done by pressing the spaces between the bronchial rings.

With regard to Dr. Tyson's remarks: I did not wish to be understood as saying that the same principle applied to the production of the laryngeal sound, for it does not. The sound to which I allude is produced only when air blows over the mouth of a tube which leads to portions of the lung where the air vesicles do not expand. We can always hear the laryngeal sound or the tracheal sound; it is one of the elements of tubular breathing. This blowing sound is transmitted to the surface of the lung and is heard externally, diminished in volume according to the conducting power of the media through which it passes. Sounds are lost very rapidly in the respiratory passages.

The point that I make is that this tubular blow is produced very near the ear and is transmitted with the same degree of intensity as a sibilant râle is transmitted to the ear.

Dr. Lyman: What value would Dr. Cary attach to the ordinary explanation that is given with regard to the difference in sound on the two sides of the chest, at the apices? One explanation is that the pectoral muscles are more developed on one side, and thus influence the sound.

Dr. Cary: I think if the muscle were larger on the right side it would rather diminish the sound. I think the true explanation is to be found in the point of departure of the upper tube going to the right lung.

THE DIFFERENT FORMS OF CARDIAC PAIN.

By SAMUEL C. CHEW, M.D.,
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Cardiac pain is a symptom belonging to several affections that differ from each other in their nature and pathology. These maladies have all the common property of pain, varying in degree and seated apparently or really in the heart. There is, however, no satisfactory term in English usage for designating this pain. On the ground of analogy, it would seem proper to call it cardialgia, after the examples of gastralgia, cephalalgia, etc.; but this word is already appropriated, illogically though it may be, to an affection with which the heart is not concerned at all. Thus, in the *National Medical Dictionary* of Dr. Billings, the first definitions of cardialgia are gastrodynia and heartburn, the last being pain in the heart. In the *Century Dictionary* and in that of Dr. Foster no other meanings for cardialgia are given than heartburn and gastralgia. Dr. Flint says that "cardialgia signifies pain at the cardiac orifice of the stomach, of a burning character;"[1] and Dr. Wm. H. Welch, in his very valuable monograph on *Ulcer of the Stomach*, says: "With most English and American writers cardialgia signifies heartburn, while continental writers understand by it the severe paroxysms of epigastric pain which we more frequently call gastralgia."[2] This usage, though fixed, is certainly contrary to etymology and to the analogy of similar words. *Heart-pain* would suggest its meaning very plainly, but it is not in accordance with English usage; for we do not say head-pain or back-pain; and if headache, backache, and earache suggest *heartache*, we are debarred from that word by the fact that since it was included with "the thousand natural shocks that flesh

[1] Practice, p. 443.

[2] Pepper's System of Medicine, vol. ii. p. 489.

is heir to," it has always been used to denote emotional rather than physical distress. We are therefore driven to the use of the terms "cardiac pain," or "pain in the heart."

This kind of pain is found as a prominent symptom principally in three different forms of disease of the heart; and I desire to refer briefly to these from a clinical rather than from a pathological point of view.

The first of these, and the one in which the pain exists in most intense degree, is angina pectoris, true angina with increased arterial tension, occurring in paroxysms, and most frequently associated with aortic or coronary disease, or with fatty degeneration of the heart. As the name of this affection implies, the pain is of the very essence of the disease itself. In severe cases it is nothing less than a mortal agony—an agony from the very intensity of the pain, and a mortal agony because, as testified by many sufferers, the pain is attended with a sense of impending dissolution. Nothing can better describe a paroxysm of angina than words used by a non-medical writer, and without reference to this disease, in which he speaks of "a sense of ruin which is worse than pain." As recorded by Dr. Latham from his own observations, it is "a suffering as sharp as anything that can be conceived in the nature of pain, including something which is beyond the nature of pain—a sense of dying." Keeping in mind this element of the paroxysms, I think Professor Flint's criticism, that "Heberden's term signifying *strangulation* has but little pertinency in this application of it," is, with all deference to his high authority, hardly justifiable: for Heberden speaks of "the sense of strangling and anxiety with which the disorder is attended"—*angor pectoris intentans vitæ extinctionem;* and he seems to use the word angina with reference to these rather than to the pain alone; to the combination of anxiety and anguish found in the disease; words, indeed, which come from the same root with angina and bear witness to the accuracy of the term as Heberden first employed it.

The structural changes connected with true angina are in a very large proportion of cases those that produce cardiac ischæmia, especially insufficiency or atheromatous rigidity of the aorta, obstruction of the coronaries, or fatty degeneration of the heart. Any one of these changes may lessen the blood-supply to the heart-muscle; but only the first two, aortic insufficiency and obstruction, are diagnos-

ticable with certainty by auscultation; we may suspect coronary obstruction or fatty degeneration, but we cannot during life prove their existence. Hence the prognosis of a case of true angina pectoris may be equally as grave where an auscultatory examination yields a negative result as where it shows organic disease; for the cardiac ischæmia on which the disease may depend may be brought about by undetectable coronary obstruction or fatty change. On the other hand, post-mortem examinations not infrequently show great sclerosis of the coronaries, and also fatty degeneration, in cases in which the symptoms of angina pectoris had not been present during life. So that it is difficult to determine what is the immediate cause of the angina, *i. e.*, what is the exact causative relation of the lesions to the symptoms.

A very common factor in the production of a paroxysm, or at least a very common attendant upon the paroxysms in the earlier attacks, is a great and sudden increase of arterial tension. Whatever be the underlying organic cause, the immediate action seems to be purely neurotic, just as it is in Nothnagel's vasomotor angina, coming on after exposure to cold, which produces apparently a spasm of the peripheral arterioles and a sudden feeling of tension or severe pain about the heart; or there may be some unknown reflex influence by which the arterial constriction and increased tension are brought about and the paroxysm excited.

It was this sudden increase of arterial tension that led Lauder Brunton, by a happy inference, to try the effect of amyl nitrite in angina. The action of this remedy in causing flushing was first observed by Guthrie, and its power of lessening tension was first shown by Gamgee, but the application of its power to the particular form of increased tension found in angina pectoris was first made by Brunton, with the well-known results of giving deliverance and safety, at least for a time, to many that have seemed ready to perish. In view of the many cases of angina in which great and prompt relief has been given by this agent, I cannot but feel surprised at the opinion expressed by several recent writers that it is doubtful whether there are any remedial agents that have the power to arrest or very greatly relieve a paroxysm of the disease. No therapeutic results seem to me more obvious and satisfactory than those that are often witnessed from the use of this remedy in angina; and I fully

agree with Professor F. C. Shattuck, that the value of the nitrites in angina is greater than Strümpell, the author upon whom he comments, would seem to admit.

A second form of cardiac pain closely allied in character to the one already considered, and yet distinct from it in its pathological relations and generally less intense in type, is encountered as a complication of some cases of chronic nephritis, chiefly the contracted kidney or interstitial nephritis. In this class of cases the changes in the kidneys, and sometimes in the heart, are parts of a general arterio-sclerosis, and the pain in the heart is probably the expression of resistance to the blood-flow through the arterioles. If it be asked why, with a constantly present mechanical cause, the attacks should be paroxysmal, with intervals between them, it may be said that this is a law of various neuroses, such as neuralgias dependent on pressure, or epilepsies due to exostosis or depression of bone, or spasmodic asthma due to nasal polypi—all conditions in which the causes are constant and the neurotic seizures paroxysmal. In this form of cardiac pain the attacks may be frequent, but they are in general less severe (such at least has been my experience) than those of true angina connected with heart-lesions. I have described several such cases in a paper read before this Association at its meeting in 1888. In all of them the symptoms of chronic interstitial nephritis existed, and in one of them, in which the painful attacks were most severe and most like those of true angina, post-mortem examination disclosed not only chronic contracted kidneys, but occlusion of the coronaries. It is in cases of this kind that potassium iodide in large doses, as advised by Huchard, may sometimes prove beneficial by lessening the arterio-sclerosis. In the painful attacks a certain degree of relief may be obtained from amyl nitrite, which, though it cannot reach the organic cause of obstruction, may lessen an incidental increase of tension.

After all, these two forms of cardiac pain may be essentially one in their pathology—both being dependent upon sclerotic changes. Regarded clinically, however, one group is composed of cases in which there are detectable or suspected organic heart-changes, with no kidney complications; while the other group consists of cases in which the kidney symptoms are always prominent, while the heart may or may not be involved.

A third form of cardiac pain is found in dilatation of the heart, and is perhaps due to tension and stretching of the nerves in the heart-substance. Traube held that the pain of true angina is due to this cause. Whether it be so or not, the subjects of cardiac dilatation frequently experience pain about the heart, greater in degree in general in proportion to the rapidity with which the dilatation is induced.

Pain may thus arise from any form of valvular disease of the heart that leads to dilatation; but of the various valvular lesions it is perhaps found most commonly in aortic insufficiency, which is likely to occasion rapid dilatation of the left ventricle, from the pressure of the backward current of blood from the aorta, at the same time that the left auricle is sending its supply into the ventricle. It is to be remembered, however, that aortic insufficiency may give rise to some cardiac ischæmia by the imperfect filling of the coronaries; and thus there may be two causes of the pain, the ischæmia and the intra-ventricular pressure. Which has the larger share in causing the pain it may be impossible to say.

If dilatation be extreme and acutely developed, free venesection may be the best means not only for relieving pain, but also for saving life.

In all forms of cardiac pain arsenic is a remedy of much value, from its action as an anti-neuralgic, and from its power of promoting the nutrition of the heart. It has no effect in the way of controlling existing pain, but it may lessen the severity and the frequency of future attacks, and I hold, with Anstie and with Balfour, that there is no more important prophylactic tonic against cardiac neuralgia than arsenic.[1]

Looking at all three of these forms of disease, and endeavoring to coördinate them as to their cause, it is quite possible that the chief factor in the production of pain common to all of them is pressure brought to bear upon the cardiac nerves or upon the cardiac ganglia themselves. The connection between these ganglia and the cervical and brachial plexuses gives a ready explanation of the extension of the pain to the arms that may occur in any form of cardiac pain. In the first or strictly paroxysmal form, true angina, the pressure may

[1] Balfour: Diseases of the Heart, p. 281.

be occasioned by the sudden tension of the arterioles; in the second form, by the general sclerotic state of the vessels; and in the third form, with dilatation of the heart, by the attenuation of the heart-walls.

DISCUSSION.

Dr. M. Allen Starr: It does not seem to me that all the cases of cardiac pain can be classified under these three heads. It seems to me that a further class should be added, and I am somewhat uncertain whether that class may not in turn be divided into several sub-classes. I am accustomed to see very intense cardiac pain in connection with paroxysmal tachycardia, of which I have seen a number of cases. In these cases there is certainly no dilatation and no hypertrophy, and the attacks differ so markedly from what is known as angina pectoris that we cannot classify them under any of the three heads Dr. Chew has mentioned. Again, in cases of extreme neurasthenia, especially in what I term the vasomotor type, where the arterial tension varies very much from time to time, where the rapidity of the heart varies very much under varying circumstances, a type of neurasthenia which can be separated from other types, I am accustomed to find patients complaining very much of pain about the heart and cardiac region. It seems to me that here we have two separate and distinct forms that cannot be included under the doctor's headings.

I would like to call attention to an article by Nothnagel in the *Zeitschrift für klinische Medicin* last year, on the subject of cardiac pain in connection with cardiac diseases. Studying a large number of cases, he found that in a fraction over 32 per cent. of cases of heart disease pain was really a symptom of the trouble.

Dr. Musser: I think we would all be better off in practice if we considered all forms of cardiac pain as angina or pseudo-angina. Dr. Chew dropped a word as to pain in the arms, and I wish he had laid more stress upon the occurrence of such pain in association with cardiac pain, or even independent of cardiac pain, as a symptom of the conditions which cause cardiac pain. I have at the present time under my care a patient suffering severe pains in both arms, without præcordial pain, but always associated with high arterial tension and other phenomena of angina.

I would like to lay stress upon the necessity of absolute rest in the treatment of all these cases, and a proper regulation of the diet—a regulation of diet based upon accurate knowledge of the actual functional disorder of the stomach that is present.

Dr. A. McPhedran: I think it is unfortunate that we have not a term to include all these cases. We meet with many cases without paroxysms which are yet true cases of cardialgia, or angina.

In regard to the treatment of these cases, I have found nitroglycerin even preferable to amyl nitrite, its effects lasting longer. I have at present a patient who has arterio-sclerosis, and suffers from præcordial pain, with paroxysmal attacks, the heart being enlarged. He is taking forty to fifty minims of the one per cent. solution of nitroglycerin daily, usually with complete relief.

Dr. Stockton: There seems to me nothing more satisfactory than to see the relatiou existing between cardiac pain and the morbid anatomy in certain cases, and nothing more disappointing than to discover the same lesions without the history of pain. Whilst this occurs not unfrequently in diseases of the coronaries, it is an extremely common thing to find dilatation without a history of pain. The claim that dilatation of the heart-muscle of the left ventricle is the chief cause of cardiac pain must be abandoned. Frequently I have watched cases in which the dilatation has been rapid, and all varieties of suffering except pain have been experienced. It seem to me that pain has not been entirely accounted for as far as the heart is concerned. That it exists more frequently with morbid changes than without them is true, but further than this we can hardly go.

Dr. Chew: Referring to the remarks of Dr. Starr, I would simply state that I did not attempt to present a complete category of all the cases in which cardiac pain might occur. I merely meant to set forth three of the most important conditions in which pain is a common symptom.

As to tachycardia, I know that it is sometimes attended with pain, but it seems to me that it is a rare condition as compared with the others, and pain associated with it is not of so frequent occurrence as it is in the other cases. Had I intended to go into a complete exposition of all forms of cardiac disease in which pain may occur I might have referred also to aortic aneurism. It is sometimes very difficult to explain how pain is brought about in this condition, although it may be a very prominent symptom.

In regard to the use of nitroglycerin: I have used it with a great deal of success in a number of cases, but it seems to me that its rôle is different from that of the nitrite of amyl; the nitrite of amyl is efficacious in giving immediate relief to the paroxysms, nitroglycerin in lessening the disposition to these paroxysms, and in lengthening the interval between them.

In the minute doses in which it is common to give nitroglycerin I have never seen it possess any power of checking a paroxysm when it has come on.

It is undoubtedly true that cases do occur in which there is dilatation of the heart, and all the physical signs, and many of the distressing symptoms of dilatation, without obvious pain; and yet we may say the same thing of other forms of cardiac lesion, such as coronary obstruction, fatty degeneration,

and aortic insufficiency. Just as in certain cases, the ordinary lesions productive of or associated with angina pectoris may exist and no angina be present, so, in some cases of dilatation, the pain does not occur.

Dr. Stockton: As to nitroglycerin and nitrite of amyl: I have in mind an instance of a man who was relieved from his paroxysms by nitroglycerin but not by nitrite of amyl. He took one-half a grain of nitroglycerin at a dose, and the effect was almost instantaneous in the relief of pain and dyspnœa. During twenty-four hours he had often taken five or six grains of nitroglycerin. The effect was magical, and I believed at first that it was to some extent psychical, but I am now convinced that it was not. The man died a month or so ago, after having had great relief from being in bed three months. In his case amyl nitrite excited but did not relieve pain. The case was one of arterial sclerosis, with very extensive left ventricular dilatation.

CROSSED PARALYSIS OF THE THERMAL SENSE WITHOUT OTHER SENSORY LOSS.

By S. WEIR MITCHELL, M.D.,
OF PHILADELPHIA.

L. B. K., aged forty-nine years. Colored. Newspaper editor. Until the attacks I shall record Mr. K. was reasonably well. He had a good ancestral history, and no record of serious disease in his own person. Some years of excessive and continuous professional toil gave rise to dyspepsia of no very grave type.

In mid-August, at the altitude of Denver, 1885, just after breakfast, not having been overheated, Mr. K. felt a severe sense of pressure at the occipital region. He was able to go up stairs, and then everything turned black, and he lost consciousness for some ten minutes. During this time his arms were said to have been rigid, but he did not bite his tongue or froth at the mouth. Is said to have had after this a distinct but slight droop of the left eyelid, and the pupil on the left was seen to be the smaller. There may be a doubt as to whether the loss of power extended beyond the lid. Dr. Lyman, to whose notes I am in debt for his early history, says: On recovering consciousness, Mr. K. had a feeling of soreness in the right leg throughout the limb, and a sense of coldness in the right arm and leg. For three weeks he could not lie on the left side without pain in the left side of the head. The left pupil remained for a time smaller than the right, and the left lid drooped. For some weeks his voice was weak and husky. At the sixth week, when seen in Chicago by Dr. Lyman, he was well save for the ptosis and the singular symptoms which came with the attack, and has remained with a history of steady gain up to this date. When seen by Dr. Lyman, Mr. K. was sallow, constipated, and had lost thirty pounds in weight. The eye symptoms were much as at first. The dynomometer showed no material difference as between the right and left hand. The tendon reflexes were exaggerated. Dr. Lyman probably refers to knee-jerks alone. The gait was unsure. Reeled when standing with shut eyes. Pulse weak; certainly no excess of tension. Heart normal. Eye grounds healthy.

Mr. K. says that except for slight numbness of left face and right leg and arm, he had no marked sensation symptoms in this direction. Touch and pain were and are appreciated duly. Shortly after the primary attack Mr. K.

found that he could not tell any degree of heat from cold on the left side of the face and on the right side of the body, leg, and arm. Cold touch was as hot contact. Both were painful if the extremes of cold and heat were used, but neither was distinguishable as a difference of temperature. This applied at first to the whole range of thermal change. After a while, and by degrees, this remarkable condition grew less notable, but in some degree has lasted up to the present date.

Mr. K. was seen by me April 21, 1892. He was as carefully examined by Dr. John Mitchell and myself as the time of a single visit allowed. Dr. John Mitchell says: I found him in perfect condition as to heart, lungs, and all abdominal organs. The urine normal. Appetite rather excessive. Digestion seems normal, but complains of a most obstinate constipation. General strength unimpaired. An active man. Station: Anterior sway one and a half inch; dextral sway one inch. Knee-jerk rather too full, but alike right and left. No clonus. Elbow-jerk normal. Muscles states, as to mechanical reactions, good. All muscle reflexes reënforceable by volitional acts and by a sensation of pain.

Sensation.—No headaches. Sense of pain, touch, taste, smell, and hearing entire. The temperature sense is still very dull on the right, except on the right face, where it is normal. The left side of the face is about as insensitive as to thermal change as is the right side of the body. Mr. K. declares that he simply cannot tell heat from cold in the skin spaces above mentioned. The difficulty ceases abruptly at the middle line. I tested Mr. K. as to the left face, arm, and hand on the right. The defect far exceeded his statement, since he had said that moderate differences could be appreciated, but I found that with two discs of metal, one hot enough to be uncomfortable to my touch and one at about 65° F., he could not say which was cold and which hot. He insisted that there was no difference unless the heat was so great as to hurt him, or the cold was kept long on the skin. In either case he complained of the pain, but could not say whether it was from heat or cold. As to all lesser variations the same rule applied. There is, too, a slight general muscular tenderness on the right side, but not in the facial muscles on the left. The nerve tracks are not tender. He thinks the dulness of the thermal sense varies. Finally, there is still slight left ptosis.

Dr. De Schweinitz says, as to the eyes, Mr. K. has decided astigmatism (which I have corrected with the corresponding presbyopic correction), and some insufficiency of the external recti. Pupils are normal. The optic nerves are of a bad color, especially on the right side, but the form and color (red and green) fields are absolutely normal; hence, the condition probably indicates some anæmia of the nerve-head, but no atrophic change. Choroid and retina normal.

Here, then, is a case of alternate paralysis of the thermal sense, and, save for the slight paresis, of this alone. The lesion must have been small in extent, and yet of a nature so situated as to cause

shock, for he became insensible and had some form of spasm. The paths of pain and touch were undisturbed. The lesion must have been on the left (there was left occipital pain) above the crossing of the thermal tracks. *The case seems to offer evidence of the existence of distinct thermal paths, and also of the fact that they cross.*

Crossed anæsthesia, which is due to disease in the upper part of the pons is rare, but has been often enough described. The classical crossed palsy of movement, etc., is more familiar. I can find no case of pure crossed thermal anæsthesia.

Since I wrote this account I have heard from K., and have the opinion given early in the case by his physician. Dr. N. A. Stedman, of Denver, says after a period of chronic torpor of liver and indigestion came abruptly the attack already described. He adds that there was some hemorrhage from the throat and the left ear, with persistent hiccough for a week. Of the amount of the bleeding I learn only this much. No mention is made of the peculiarity as to sensation. It certainly was known almost at once, or within a day or two.

The thermal dysæsthesia still exists. At first it was complete; now Mr. K. finds that it requires thirty to forty degrees of difference of temperature to enable the right hand to say which is cold. Beyond that discrimination is easier, but mistakes may be made.

Finally, the slight muscular hyperæsthesia is to be noted, pressure causes annoyance, and this is not in nerve tracks, but about joints and bones as well as muscles. Horse exercise makes the muscles on the right side of the body sore and also the left side of the brain. If, as is not rare, he has an acid stomach, the whole right side is too sore to lie upon. The pain in the left ear and back of it to the middle line were frequent for three years, but now are gone; but above all else is he dependent for comfort upon freedom from acid states of body.

The above case probably stands alone in medicine. It seems to prove, as I have said, that there are separate thermal nerve tracks, as to which I have hitherto doubted. Also it seems to make sure that these tracks cross.

TUBE-CASTS AND THEIR DIAGNOSTIC VALUE.

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THE study of renal tube-casts is nothing new. Since Henle, in 1842, first comprehended and announced their importnace, their relation to renal diagnosis and pathology has been generally admitted. The exhaustive essay of Bartel in Ziemssen's *Cyclopædia* is an excellent record of our knowledge of casts up to that time; but I think something more may now be added.

For some years past I have had occasion to study tube-casts frequently and consecutively for purposes of diagnosis, and while doing so have insensibly, perhaps, arrived at certain results and reached certain conclusions, which it is my purpose to set forth in this paper. I do not claim any new discoveries, but hope my paper will add something of system and definiteness to the study of casts and something of certainty to the diagnostic conclusion drawn therefrom.

Concerning the origin of tube-casts, I think they are clearly of two distinct kinds, each having a different origin and each indicating a different pathological process.

First, we have the mucous, or more properly mucin, casts, and I do not think this variety has received the consideration to which their importance entitles them. The mucin casts I would divide into two groups.

(*a*) Simple mucin casts without crystalline or cellular elements.

(*b*) Casts which include saline or cellular elements acquired during their formation in the kidney. This division has an important bearing on diagnosis, as I shall endeavor to show presently.

Secondly, we have the true fibrinous casts, or those which have

long been recognized and variously classified by different writers—which may be divided into four groups:

(*a*) The hyaline "structurelesss" casts, which contain no formative elements whatever.

(*b*) Blood-bearing casts.

(*c*) Cell-bearing casts.

(*d*) Fatty casts.

This classification may be reduced to tabular form for purposes of systematic study as follows:

Class I. Mucin Casts.

(*a*) Simple mucin casts entirely destitute of formative elements.

(*b*) Mixed mucin casts or those which include crystalline or cellular elements acquired during their formation in the tube.

Class II. Fibrinous Casts.

(*a*) Hyaline or structureless casts.

(*b*) Blood-bearing casts.

(*c*) Cell-bearing casts.

(*d*) Fatty casts.

Of course, each group may be divided into sub-groups, but such wire-drawn distinctions serve no good practical purpose, while they are likely to confuse and perplex the student.

Mucin Casts.—Turning now to the First Class, the *mucin cast*, let us consider its origin and pathological import. It is certainly not the product of an exudate, and is therefore not directly derived from the bloodvessels, and this fact separates it at once and forever, as regards origin and pathology, from the fibrinous cast, a point I shall allude to again presently.

It is undoubtedly true that the mucin cast is formed within the renal tubules and from material furnished by the tubal epithelium of the convoluted tubes. Under certain circumstances the epithelial cells seem to undergo a change equivalent to the "mucoid degeneration" of Ziegler, the protoplasm of the cell being transformed into mucoid substance, which is afterward cast into the lumen of the tubule, there to aggregate itself with the similar product of neighboring cells, thus forming the simple "mucin cast," or the long, wavy string of mucin so often seen in urine. It is the product of a catarrhal nephritis,

a pathological state to be sharply differentiated from exudative nephritis, with relation to origin, treatment, and results.

I have contended for more than ten years that "catarrhal nephritis" ought to have a distinct recognition in our systematic nosology, simply because it *is* a distinct disease, frequently existing for years, and having its own characteristic symptoms and course. The simple mucin cast is the characteristic morphological product of this disease and establishes its differential diagnosis. Frequently it is the only reliable indication of the existence thereof, since catarrhal nephritis is not generally accompanied by subjective symptoms of any marked significance.

Along with the mucin cast are frequently found tubal epithelium, leucocytes and urinary salts, but these have no necessary relation to the pathological condition indicated by the mucin casts; it alone establishes the diagnosis of catarrhal nephritis.

The "*mixed*" *mucin cast* is the "simple" mucin cast plus whatever crystalline or cellular elements may chance to be present. Clinical experience shows that the elements most likely to be present are leucocytes, or crystals of lithic acid, or oxalate of lime. If the former be present it shows that there exists a catarrhal condition of sufficient intensity to induce rapid multiplication of the nuclei of the epithelium, which by reason of the "mucoid" degeneration of the protoplasm of these cells are set "free" and are hence easily enclosed in the mucin cast during its formation.

It may be said that these leucocytes are the consequence of diapedesis; but if that were true we should have hyaline (fibrinous) casts instead of mucin casts, since we cannot conceive of a hyperæmia sufficient to produce diapedesis without at the same time inviting exudation.

Of course, if hyaline casts *are* present, exudation is proven, and the diagnosis of exudative inflammation is thereby established. It is not at all unlikely that hyaline and mucin casts may exist together, which would show that the case was in a transition state from catarrhal to exudative, or *vice versa*, as I have seen in many instances; and it is in just such cases as these that familiarity with the appearance of tube-casts and their diagnostic pointings is so necessary, since it is impossible to establish a refined diagnosis from any other standpoint.

When the mucin cast includes crystals of lithic acid, oxalates, or phosphates, it is clearly correct to assume that these crystals were deposited in the renal tubule, and that they point to a diathetic condition which determined their formation.

From a diagnostic point of view, it is important to note that the crystals are *within* the cast and not adherent to its *surface*; because it clearly warrants the conclusion that they were formed in the renal tubule and not in the pelvis or bladder.

This being the case, we can readily account for the renal irritation which has led up to the renal catarrh and consequent renal inadequacy, so common when these diathetic factors are encountered. The diagnostic value and the importance of recognizing these crystals, and of determining their nature and location, is thus clearly indicated.

In the year 1874, and again in 1879 and 1880, the late Dr. Mahomed drew attention to "high arterial tension" as a symptom prophetic of chronic interstitial nephritis, and described what he designated as the "pre-albuminuric stage" of Bright's disease. His writings attracted wide and well-merited attention, but his untimely death occurred before he had completed his researches and experiments. It was his belief that "high tension," or irritable heart with contracted and resistive bloodvessels, preceded albuminuria sometimes for months or even years. It was his further belief that the approach of renal cirrhosis might be predicted by carefully estimating the degree and constancy of cardio-vascular tension, by means of consecutive sphygmographic tracings. A broader study of this subject has developed the fact that this peculiar condition is not certainly present, except in cases of well-marked lithæmia, and that even then, as Dr. Grainger Stewart has observed, some degree of cirrhosis usually precedes the symptom.

Increased or abnormal vascular tension, then, can hardly be regarded as a prophetic or prodromic symptom of renal cirrhosis, although its value as regards differential diagnosis cannot be denied. But I believe the presence of the mucin cast is of far greater diagnostic value than high arterial tension under any circumstances.

In the first place, I am satisfied that the great—in fact, the overwhelming—majority of cases of interstitial nephritis are preceded by a long period of faulty digestion and mal-assimilation. That is

certainly the case in the city and vicinity of Chicago, where my observations are chiefly made. This leads to overworked and irritated kidneys, as Dr. George Johnson first pointed out; but more than that, it leads to the development of renal catarrh, as Dr. Johnson did *not* point out.

Vitiated or abnormal urine produces a catarrhal irritation of the kidneys, just as vitiated or abnormal ingesta produce a catarrhal irritation of the stomach. The next event is the appearance of the mucin cast long before any recognizable renal lesion occurs, and long before arterio-capillary tension is present in such degree as to be detected, except by the most expert and experienced sphygmographist. In fact, arterio-capillary tension as a practical everyday symptom for the guidance of the ordinary practitioner, does not yet possess the value which Mahomed, as well as Gull and Sutton, predicted for it. Its recognition presupposes the possession of instrumental and technical knowledge not generally possessed by those most likely to encounter the cases to which they are applicable. Moreover, as I have already said, the symptom in question does not usually precede the lesion which it indicates. Again, vascular tension does nothing more than suggest a possible diathetic antecedent, whereas it is all-important, if such a complication be present, that it be promptly recognized and appropriately treated.

I claim for the mucin cast a position of preëminent importance in the early diagnosis of interstitial nephritis; more than this, I claim that the appearance of the mucin cast is a prophecy of that change which is only too sure to follow chronic catarrhal nephritis.

Moreover, the cause or "diathesis" which preceded and led up to the catarrhal kidney may generally be detected by the microscopic study of the urinary sediment which falls down along with the casts, and as this "diathesis" includes or rather *is* the essential pathological factor in a given case, its early recognition is most important. And all this can be done—is daily being done—by him who is most concerned in all our researches and experiments, namely, the general practitioner. And what seems to me a consideration of no small importance is the fact that the recognition of the mucin cast and the crystals or granules of lithic acid are not matters of opinion or guesswork, or a question of comparative judgment, but simply a question of fact, and of fact only; these objects are present or they

are not, and that settles it. But the degree of arterio-vascular tension in a given case is a matter of comparative judgment at best, and in every case is a very variable factor, present to-day and absent to-morrow. It is proper, although perhaps needless, to add that the foregoing statements are based on a long and cumulative experience, and are in no proper sense theoretical or conjectural, but are based upon long and careful study of many cases, some of which are still under observation.

Fibrinous Casts.—I will now ask your attention briefly to the second class, namely, the true fibrinous casts. The presence of the fibrinous casts in urine is abundant proof that sufficient hyperæmia has existed in the kidneys to produce exudation of the fibrin factors and most probably diapedesis. It is proof, therefore, of the presence of "exudative" inflammation, instead of "catarrhal" inflammation, which I have just considered. I regard it as very essential that this distinction be kept in mind, since it has much to do with the question of treatment, and is all-important in its relation to prognosis. In both forms of disease albumin may be present; in both forms it may be present at one time and absent at another; and in the early stage of exudative (interstitial) nephritis the quantity may be so small as to require very careful testing to prove its presence. In catarrhal nephritis the amount is always very slight, many times amounting to no more than a trace. As a diagnostic symptom, therefore, albumin has very little value and no uniform value. But tube-casts have a positive as well as uniform diagnostic value, provided their language is understood, and one of the most important points settled by them is the question whether, in a given case, we are dealing with catarrhal or exudative inflammation.

The *hyaline cast*—the first variety of the second class—is the simplest and most innocent form produced by exudative nephritis. It is so small and so translucent that it frequently escapes detection, unless the examination happens to be made by an expert microscopist. Its diagnostic value depends upon its frequency and upon its form and symmetry. If only an occasional hyaline cast is found it goes to show that exudation is very slight; that it is in its incipiency, or has well-nigh ceased, a question which can easily be decided by reference to other symptoms which do not come within the scope of this paper. If many are present, exudation is still going on

actively. In my own examinations I lay great stress upon the form of the cast; if it is smooth and symmetrical, or free from "twists" or distortions, it seems to me to prove that it was formed in a tube not yet distorted by the encroachments of pathological connective tissue; but if the cast is not smooth and regular on its surface, and if it shows angularities, as though it had been violently bent or twisted, I am equally confident that the cirrhotic process has already made considerable progress. I regard this as a very important diagnostic indication, and one which has helped me greatly in seeking grounds upon which to found a reasonable prognosis. It will save repetition, if I say now and here, that the same observations with reference to symmetry and form apply in equal degree to the varieties of casts which are yet to be mentioned.

Blood-bearing casts indicate a hyperæmia sufficient to cause hemorrhage into the renal tubules, although it may be very slight indeed. Hence blood-casts are commonly regarded as proof of acute nephritis and of that only. But in every such case it should be borne in mind that while the blood cast may be the immediate result of an acute lesion, a long-standing chronic lesion may have preceded it, and careful search for other forms of casts should be made. In other words, a prognosis founded upon blood casts alone is quite likely to disappoint the expectations of physician and patient. In every case of apparent acute nephritis careful search should be made for casts which indicate preëxisting chronic disease, and it is not wise to prognosticate favorably until several consecutive examinations have failed to reveal the casts of chronic nephritis. I have rarely met with cases of so-called "idiopathic" acute nephritis which were not preceded by undoubted chronic nephritis.

Cell-bearing casts, the "epithelial casts" of authors, are so common and are generally so well understood that little need be said about them, except to emphasize two or three points. Care should be taken to determine whether the cells adhere to the surface of the cast or whether they are incorporated therein. In the former case they may not be the result of pathological exuviation, but they may represent only the wasted cells which are the result of wear and tear, and whose escape has been anticipated slightly by the friction of the cast as it passes down the tubule; in the latter case they must have fallen off from purely pathological causes. The shape or form of

cell casts is as significant as that of hyaline casts. Casts from a cirrhotic kidney are liable to be twisted and distorted; casts from a case of tubal nephritis are likely to be straight, symmetrical and rather large. In either form the cells may be cloudy, granular, or filled with glistening droplets of fat, thus indicating with great precision the stage or condition of the case under examination, as the more advanced the process of fatty degeneration of the cells the more advanced the destruction of the kidney in which they were produced.

Fatty casts are evidence of the completion of the destructive process of which the hyaline casts witnessed the beginning. They are more or less numerous as the case is more or less advanced in its ultimate pathological history. They are more or less eroded and roughened as the tubule is more or less denuded of its epithelial lining, and otherwise roughened in its lumen. They are more or less twisted and distorted as the tubule is more or less pulled out of shape and symmetry by the encroachments and contractions of the pathological connective-tissue. Thus they indicate the stage as well as the form or type of the disease of which they are the product. With fatty casts may be mingled hyaline and epithelial casts; in fact, the three forms are frequently found together. The stage of the disease in a given case would be pretty accurately indicated by the predominating type of cast; but at the same time it would be evident that some minor portion of one or both kidneys was either more or less advanced in pathological change than the chief portion of these organs.

I have not regarded the *waxy* or *amyloid* cast as entitled to a separate grouping, because it is only an accidental variety of fibrinous cast, presenting no inherent peculiarities of structure, and therefore indicating no pathological changes in the kidney which are associated with its presence. Waxy casts are almost invariably hyaline or structureless; if they happen to contain the peculiar waxy or amyloid material implied by their name the iodine test will promptly demonstrate it, and thus establish the diagnosis of waxy kidney; but clinical experience shows that the amyloid disease can seldom be differentiated in this manner.

In conclusion, permit me to add that I have long been persuaded that the course of a given case of acute or chronic nephritis; the type of the disease; the sequence and nature of the pathological events

taking place in the kidneys; and the ground for a reasonably positive prognosis, may be evolved from an intelligent and careful consecutive study of the tube casts alone. Other factors, of course, enter into the diagnosis, and their value and importance I do not question; but I believe, with Formad, of Philadelphia, that the tube-cast conveys more actual and accurate information to the practical microscopist than any or all other symptoms or signs.

REPORT OF A CASE OF GLANDERS, WITH RESULTS OF BACTERIOLOGICAL STUDIES.

By WILLIAM PEPPER, M.D.,
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C. M., aged fifty-five years, a native of Germany, and by occupation a shoemaker, was admitted to the University Hospital, October 1, 1891. It was impossible to obtain a satisfactory family history. His parents, brothers, and sisters were all dead, from causes unknown to the patient.

He has always been healthy until eighteen days ago; but has drunk to excess for many years. His occupation did not bring him into contact with horses or mules, nor is there any history of such contact. He had to handle leather, but he thinks there has been nothing whatever unusual in its character of late.

He attributed his illness to working in a damp cellar during the past year. On September 10th he first noticed two irregularly shaped, indurated, and

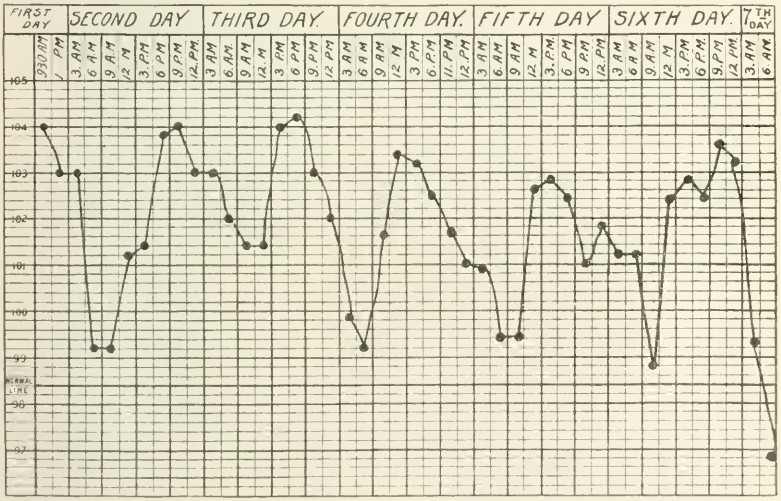
Fig. 1.

painful nodules under the skin, one on the right leg, the other on the left arm. The appetite became poor, and there were several loose stools daily. Ulceration was abnormally frequent, and he thinks the amount of urine was decidedly increased. On admission the patient was dull and heavy. The

temperature was elevated. The pulse was rapid and weak, and the respiration hurried. There were a number of masses under the skin; one tumor in each calf, one in the right thigh, one in left gluteal region, one in left wrist, two in right arm, and several about the cheeks and nose. All the masses were of variable size, from a half-inch in diameter up to three by two inches, and with corresponding differences in depth. Over some of them the skin was normal, in others it was reddened, and in several places it was ulcerating. On October 2d and 3d there was no change in the symptoms, and he was apparently more comfortable. The urine contained neither sugar nor albumin. On October 4th he was decidedly worse. His expression was that of profound intoxication. There was muttering delirium, with deepening hebetude. There were coarse crackling râles on deep inspiration at the left base posteriorly. No cardiac murmurs. Splenic dulness was distinctly increased. The tongue was dry, parched, and fissured. There was a pustular formation at the right ala of the nose, and the face was markedly œdematous. (See Fig. 1.)

On October 5th there were marked carphologia and subsultus. The urine was passed involuntarily, and now contained a trace of albumin. Several new nodules had appeared. The ulceration had spread at the points where

Fig. 2.



it had begun, and these nodules were breaking down. On the other hand some nodules, over which the skin was not reddened, now disappeared and others were distinctly smaller. Examination of blood showed 80 per cent. of hæmoglobin; the red corpuscles 4,800,000, with a moderate degree of leuco-

cytosis. The red corpuscles were of normal size, shape, and color. No microorganisms were detected in the blood.

On October 6th the patient was in deepening coma. There was more albumin in the urine. The leucocytosis was much more marked. No microorganisms could be detected in the blood. The examination of the blood was made by Professor Guitéras and Dr. Daland. A vesicular eruption appeared at various parts of the body. The temperature was very irregular, and showed rapid variations of from 3° to 5°. It fell to subnormal 96.6° toward the end. The maximum was 104.2°. (See chart, Fig. 2.) Death occurred on October 7th, about twenty-five days after the first nodules were noticed.

I append the reports of Dr. John Guitéras, Professor of Pathology and Morbid Anatomy in the University of Pennsylvania, and of Dr. William M. Gray, of the Surgeon-General's Office, Washington, who were kind enough to undertake careful pathological and bacteriological studies of the case.

Report on the Microscopic and Experimental Examination, by PROFESSOR JOHN GUITÉRAS.

1. *Examination of blood during life.* On October 5, 1891, four cover-glass preparations of blood were made and stained with fuchsin, and with Loeffler's methyl-blue. A single diplococcus group was found in one of them. This was probably the result of accidental contamination. A considerable degree of leucocytosis was observed. On October 6th a second examination of the blood gave negative results as to bacteria.

Culture experiments. Two gelatine tubes were inoculated with blood obtained by puncture of the skin. Rolled gelatine tubes were prepared from one, and agar plates (glycerine agar in Petri dishes) from the other. The dishes kept in the incubator at a temperature of 37° C. remained sterile. One rolled tube contained a colony of tetragonus.

2. *Examination of pus from cutaneous and subcutaneous nodules during life.* October 5th. Cover-glass preparations were made from a cutaneous abscess already opened, and from a deeper-seated nodule opened for the experiment. These were stained with a mixture of eosine and methyl-blue. The first preparations contained, besides pus cells and detritus, some micrococci and very few bacilli. The deeper abscesses contained bacilli among the pus cells. In one preparation five were counted and seven in another. The description of these corresponds morphologically with that of the glanders bacillus.

3. *Culture experiments.* Two sets of agar plates (glycerin agar in Petri dishes), three in each set, were prepared from the pus of a deep-seated abscess. The agar here employed coutained 1.5 per cent. of agar and 4 per cent. of glycerine. The temperature of the incubator was kept at about 37° C. The growth of colonies was very scanty. These represented a minute micrococcus and the bacillus already described. The latter was grown again

upon agar and upon potato. The growth upon agar was mixed with the micrococcus. A characteristic honey-like growth was obtained upon potato. Again the bacillus in this was shown to be morphologically identical with the glanders bacillus.

4. *Inoculation experiments.* A rabbit was inoculated subcutaneously in the back with pus from the subcutaneous abscess suspended in water. The rabbit had some fever on the fifth day after the inoculation, and a local inflammatory reaction which lasted three days. The animal recovered.

5. *Post-mortem examination of the patient, C. M., three hours after death.* Body of a robust man weighing 140 pounds. Rigor mortis just commencing. Slight cadaveric lividity in the back of the neck. The skin of the face, trunk, and extremities presents a bullous eruption. Fifty vesicles can be counted over the front of the trunk. Some of these contain a straw-colored fluid, whilst others present a purplish color. The vesicles are formed by liquefaction of the superficial layers of an indurated base which extends to the papillæ. Some of the bullæ are surrounded by crops of smaller vesicles. Seventeen vesicles are counted on the left, and twenty on the right arm. The number is less on the lower extremities. There is a gangrenous ulcer on the outer surface of the right thigh, with excavated borders. It does not penetrate the deep fascia. Another ulcer in the calf of the left leg measures seven by three and a half centimeters. It presents the same excavated edges, and penetrates into the muscle. Some vesicles are found on the face, as well as some ulceration about the alæ nasi and the masseter region.

In many places where no lesion of the skin is apparent, deep-seated nodules about the size of a split pea, and larger, can be felt. On cutting into these they are found to contain a cheesy material which shows frequently a tendency to break down in the centre. The base of the vesicles is formed of the same material.

Thorax. The pleuræ are not adherent, and the cavity contains no fluid. The pericardium is the seat of old adhesions, which, though light, nearly obliterate the cavity. Under the visceral layer there is an excess of fat.

The heart is flabby and infiltrated with fat. The muscle is dark in color, and otherwise healthy. The endocardium is slightly thickened in patches. The valves are normal. The organ weighs 390 grammes.

Left lung. The lower lobe presents numerous patches of lobular pneumonia, varying in size from a millet seed to a filbert. In some of them the centre is undergoing cheesy change. There is acute bronchitis. The larger tubes present some miliary deposits, and the smaller tubes contain pus. The surface of the lung is marked with subpleural fibrous nodules containing pigment. The right lung is anæmic. The bronchial lesions are much less marked. The subpleural nodules are also present. The bronchial glands are soft, dark, and very slightly enlarged, but they show no deposits.

A few miliary cheesy nodules are found in the ary-epiglottic folds. The soft palate and fauces are swollen and œdematous. The velum presents upon the nasal surface a round ulcer, with cheesy floor, and measuring three milmeters in diameter. The cervical lymphatic glands are slightly enlarged.

Abdomen. The spleen measures 17 by 10 by 2.8 centimeters. The capsule and substance are normal. The lymphatic follicles are somewhat prominent.

Kidneys. Left kidney measures 12.5 by 7 by 3.8 centimeters. Weight 210 grammes. The capsule is slightly adherent. The consistency is normal. The cortex is anæmic. Two minute cysts are found on the surface. The right kidney measures 12.2 by 6.8 by 3.5. Weight 110 grammes.

The supra-renal bodies are normal.

The intestinal mucous membrane is swollen and œdematous throughout, and very red in some places. The stomach and pancreas are normal.

Liver. Measures 35 by 17 by 10 centimeters. Weight 2100 grammes. The capsule is thickened and opaque in patches. The consistency of the organ is increased, and the surface is slightly uneven. The upper surface of the left lobe shows scattered yellow nodules, two and three millimeters in diameter. These contain a creamy thick substance. On the lower surface of the same lobe several of them have run together, forming an abscess cavity the size of a walnut. It contains the same thick white pus. The liver substance is of a uniform brown color.

The pelvic organs and the testicles are normal.

The brain and membranes showed nothing abnormal, except that the latter were somewhat congested and œdematous.

Muscles. Circumscribed abscess cavities, about the size of filberts, were found in the lower extremity of the left deltoid, and in the middle of the right biceps. In both arms there is a diffuse disintegration of the lower third of the triceps. The contents of these muscular abscesses consist of a dark, reddish-gray, grumous fluid.

The humerus and femur were examined and found normal.

A microscopical examination of the lesions showed everywhere evidence of inflammation. There was multiplication of cells and migration of cells toward the focal centers. The earlier stages of this process could be best studied in miliary lesions found in the infundibular septa of the lung and in the bronchial mucous membrane, where the round cell infiltration had not yet completely hidden the groups of epithelioidal cells. In later stages the round cell infiltration was extensive and compact. The polynuclear round cells were very numerous, but the process of liquefaction of the intercellular substance and the formation of pus was comparatively slow. As regards the tendency to liquefaction it has been said with propriety that these lesions occupy an intermediate position between common suppuration and tuberculosis.

The bacilli of glanders were sparingly found in some of these lesions. They were not found in the muscular abscesses. Very few were found in the liver. They were most readily found in the skin and in the pulmonary lesions.

6. The following *culture and inoculation experiments* were instituted at the autopsy.

Culture experiments made with the blood in the right heart gave negative results.

Culture experiments with the pus obtained from the subcutaneous nodules resulted in the successful cultivation of the bacillus previously mentioned, upon glycerin, agar, and potato. The characteristic features of these were those of the glanders bacillus. Occasionally, however, these cultures were found to be contaminated by the same minute micrococcus found in the cultures made during life. This micrococcus is separated with difficulty from the cultures of glanders, and presents features that distinguish it from the ordinary bacteria of suppuration. As will be seen further on, the pure cultures of the bacillus thus obtained, furnished the material for the successful inoculation of guinea-pigs, thus establishing beyond question the diagnosis of glanders.

7. A rabbit was inoculated with the creamy material taken from a subcutaneous abscess under the skin near the root of the ear. The rabbit remained sound. There was no local lesion.

A third rabbit was given an intravenous injection containing four drops of blood obtained from the heart. The rabbit remained sound.

8. *Inoculation experiments made with the pure cultures* mentioned in paragraph 6.

Guinea-pig No. 1. Large female. The creamy material from the interior of a subcutaneous nodule opened at the autopsy was cultivated upon potato, after Globig, at a temperature of 37° C. The characteristic honey-like growth was obtained. On October 12th the guinea-pig was inoculated from one of these potatoes (fifth-day growth), in a subcutaneous pocket made in the right groin. On October 17th some induration was noticeable. On the 22d there was a superficial ulcer upon a hard base at the seat of inoculation. On the 27th, two secondary areas of induration were noticeable, one in the lymphatic glands of the corresponding groin, the other in the neighboring mammary gland. No general disturbance. November 1st, induration of the mammary gland became adherent to the skin, and the latter began to be involved in the necrotic process. The lymphatic glands of the opposite groin became implicated. Some loss of flesh was noticeable, and the temperature was elevated. There was no nasal discharge. Death occurred on November 6th.

Post-mortem. The mammary abscess had extended considerably in the abdominal wall, involving the muscle. The cavity was not circumscribed, and it contained a brownish pultaceous fluid. At the right groin there was a glandular enlargement of the size of a chestnut, the centre of which could be easily broken up into a pulpy mass. A pocket of smaller size was found in the left groin.

The lumbar, and, to a less extent, the bronchial glands were enlarged. The spleen, the liver, and the kidneys presented numerous yellow miliary nodules, most of which were very small. The kidneys were decidedly enlarged. The bladder was distended. There was an extensive lobular pneu-

monia, distributed irregularly throughout both lungs, and involving about one-half of them. The affected areas were very dark in color, and they exuded a sanguinolent fluid. A few minute grayish nodules were seen in these areas.

All the circumscribed nodular lesions described present the same characteristics, namely, a cheesy centre, around which are seen here and there epithelioidal cells and an extensive round-cell infiltration. The line of demarcation between the necrotic centres and the areas of proliferation is very diffuse. We do not see those ridges of vesicular nuclei that so frequently mark the boundary of the caseous areas in tuberculosis, but we have rather the evidences of a more acute process with tendency to suppuration. This is shown also by the large number of polynuclear cells, or rather cells with fragmented nuclei.

The pulmonary lesions are those of catarrhal pneumonia. In some places the air vesicles are free from exudation, and a minute nodule has formed in the point where the septa meet. These interstitial bodies offer the best opportunity to study the epithelioidal cells and the nuclear division. The bacilli are less numerous in the pulmonary lesions than in the other organs. They are never very numerous, and they are found among the cells. The most satisfactory method of staining is that of Kühne, by means of carbol-methyl-blue. Very weak solutions of acetic or muriatic acid are used for differentiation, and the section is dried upon the slide before mounting.

Guinea-pig, No. 2, a large male, was inoculated on October 31st, from a potato-culture twice removed from the original. The history of this experiment is very similar to that of No. 1, except that there was no abscess of the mammary gland, and that the retro-peritoneal glands were more extensively involved.

10. *Probable inoculation of the human subject.*

Whilst engaged in these manipulations the hands of the experimenter were accidentally abraded on October 17th. About the 24th a small pimple was noticed on the back of the hand. Considering the possibility of infection and the indolent character of the little tumor, it was removed by Dr. J. William White on October 30th. He describes the growth as a "small indolent tubercle extending from the surface to the subcutaneous connective tissue, not surrounded by an area of congestion or inflammation, and apparently consisting of sluggish granulation tissue." The small tubercle was removed with the surrounding healthy tissue. The wound, about 1.75 centimeters long, healed very slowly (about six weeks), and the healing was attended with much induration. No secondary manifestations have shown themselves. On microscopic examination the nodule was found to be made up of granulation tissue with a necrotic centre. A few bacilli corresponding in form with the glanders bacillus were found in the centre.

One-half of the nodule was further experimented with. All cultures and direct inoculations into guinea-pigs failed completely. The nodule was proven to be sterile. The reason of this very probably is, that the skin had been

thoroughly washed with bichloride solution before the operation, and that the tissue removed lay for about twenty minutes in the folds of a towel wet with the same solution.

Dr. William M. Gray kindly furnished me with photographic reproductions of the bacilli found in the blood from the end of a finger, and of pure culture obtained from one of the subcutaneous nodules. He pointed out that most of the bacilli looked as though they were spore-producers. Although many eminent authorities believe that their appearance is due to shrinkage, and that bacilli do not produce spores, Dr. Gray is inclined to hold the opposite opinion. He states that he has examined them under so many different conditions, and has always detected them in this stage, so that it is hard for him to believe they are not spore-producers.

INDEX.

Abscess, hepatic, 181
Alcoholism, treatment of, 62
Anæsthesia, local, as a guide in the diagnosis of lesions of the lower spinal cord, 223
Atkinson, treatment of typhoid fever by cold baths, 5, 9
quinine in malarial hæmaturia, 295

Bacteriological researches, practical results of, 68
study of drinking water, 1
Ball, dysentery, 141
Baths, treatment of typhoid fever by cold, 44
Breathing, tubular, in consolidation and other conditions of the lungs, 313

Cardiac pain, different forms of, 324
Cary, Landry's paralysis, 221
tubular breathing in consolidation and other conditions of the lungs, 313, 322, 323
Casts, tube-, and their diagnostic value, 335
Chew, different forms of cardiac pain, 324, 330
Chorea and rheumatism, seasonal relations of, 249
Consolidation of the lungs, tubular breathing in, 313
Councilman, dysentery, 113

Dabney, abscess of liver, 181
Danforth, tube-casts and their diagnostic value, 335
Dysentery, 113, 141
treatment of, by irrigation, 169

Garland, treatment of alcoholism, 67
Gastric research, misconceptions and misnomers revealed by modern, 300
Glanders, report of case of, 344
Griffith, mitral systolic murmurs, 102
tubular breathing, 321

Hæmaturia, malarial, 281
Hæmoglobinuria, malarial, 281

Hare, quinine in malarial hæmaturia and hæmoglobinuria, 281, 299
tubular breathing, 321
Heart pain, different forms of, 324
Henry, quinine in malarial hæmaturia, 298
seasonal relations of chorea and rheumatism, 263
Hepatic abscess, 181

Intermission, significance of, in functional nervous disease, 267
Irrigation, treatment of dysentery by, 169

Jacobi, seasonal relations of chorea and rheumatism, 264, 265
Johnston, treatment of dysentery by irrigation, 169

Kinnicutt, practical results of bacteriological researches, 85
treatment of typhoid fever by cold baths, 57
tuberculin in tuberculosis, 99

Landry's paralysis, 212, 215
Latimer, treatment of alcoholism, 62, 67
Lewis, seasonal relations of chorea and rheumatism, 249, 266
Liver, abscess of, 181
Loring, quinine in malarial hæmaturia, 296, 298
Lyman, practical results of bacteriological researches, 86
seasonal relations of chorea and rheumatism, 265
treatment of gastric disorders, 312
tubular breathing, 322, 323

Malarial hæmaturia and hæmoglobinuria, 281
Mason, tubular breathing, 320
McPhedran, Landry's paralysis, 215
Miles, Landry's paralysis, 212
local anæsthesia in the diagnosis of spinal lesions, 248
Mitchell, crossed paralysis of the thermal sense without other sensory loss, 332
local anæsthesia in the diagnosis of spinal lesions, 248
seasonal relations of chorea and rheumatism, 263
Mitral systolic murmurs, 102
Murmurs, mitral systolic, 102
Musser, different forms of cardiac pain, 329
seasonal relations of chorea and rheumatism, 266
treatment of gastric disorders, 311

Nervous disease, significance of intermission in functional, 267

Osler, treatment of alcoholism, 67
of typhoid fever by cold baths, 57

Paralysis, Landry's, 212, 215
of thermal sense, crossed, without other sensory loss, 322
Pepper, report of case of glanders, 344
treatment of typhoid fever by cold baths, 58

Quinine in malarial hæmaturia and hæmoglobinuria, 281

Rheumatism, seasonal relations of chorea and, 249

Spinal cord, local anæsthesia in the diagnosis of lesions of, 223
Starr, different forms of cardiac pain, 329
local anæsthesia in the diagnosis of spinal lesions, 223, 248
seasonal relations of chorea and rheumatism, 262
Sternberg, bacteriological study of drinking-water, 40
practical results of bacteriological researches, 68, 86
Stockton, different forms of cardiac pain, 330, 331
misconceptions and misnomers revealed by modern gastric research, 300 312
quinine in malarial hæmaturia, 297
treatment of typhoid fever by cold baths, 61

Thermal sense, crossed paralysis of, without other sensory loss, 332
Thompson, treatment of typhoid fever by cold baths, 59
Thomson, Landry's paralysis, 222
seasonal relations of chorea and rheumatism, 265
significance of intermission in functional nervous disease, 267
Trudeau, tuberculin in tuberculosis, 87
Tube-casts and their diagnostic value, 335
Tuberculin in tuberculosis, 87
Tuberculosis, tuberculin in, 87
Typhoid fever, treatment of, by cold baths, 44
Tyson, quinine in malarial hæmaturia, 296
treatment of typhoid fever by cold baths, 60
tubular breathing, 320

Vaughan, bacteriological study of drinking water, 1, 40, 42
practical results of bacteriological researches, 85
quinine in malarial hæmaturia, 298

Water, bacteriological study of drinking-, 1
Welch, bacteriological study of drinking-water, 40
practical results of bacteriological researches, 84
tuberculin in tuberculosis, 101
Wilkins, treatment of typhoid fever by cold baths, 44, 61

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